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VOLUME 224 MAY 29, 1941 NUMBER 22

DANGERS OF RADIATION WITHOUT BIOPSY OF BRAIN TUMORS IN CHILDREN*

Report of a Case

FRANC D. INGRAHAM, M.D.,† AND JAMES B. CAMPBELL, M.D.‡

BOSTON

THE following case report is presented in the hope that similar disastrous results may be avoided. The patient had a good prognosis in other respects, but the resulting total and permanent blindness in this case is owing, we believe, to the fact that radiation was performed for over two years in the mistaken belief that the brain tumor was a medulloblastoma. The practice of radiation without biopsy and decompression has been carried out to a considerable extent in and about Boston (seldom elsewhere) since the presentation in 1935, and publication in 1936, of a rather convincing paper[1] advocating this method of attack. There is no doubt whatever that in many cases the diagnosis thus made is correct, that the patient is spared the ordeal of exploratory operation, and is as well off in the end. We are convinced, however, that even one case similar to that presented here is sufficient reason for discarding any method of treatment that makes such a result possible.

CASE REPORT

An 8-year-old girl entered the Children's Hospital with a complaint of headache, vomiting and unsteadiness of gait of more than 2 years' duration. Two months after the beginning of her illness, she entered another hospital complaining of headache and vomiting; examination showed poor reaction of the pupils to light and accommodation, hyperactive reflexes and a sustained right-ankle clonus. The history and signs suggested a mid-line cerebellar tumor, and a diagnosis of medulloblastoma was made and x-ray therapy recommended. The patient was given radiation as follows: at the beginning, 600 r to each side of the head; 4 months later, 600 r to these areas, 600 r to the posterior field directed at the cerebellum, 600 r to the cervical dorsal spine and 600 r to the dorsal lumbar spine; 6 months later, 600 r to each of the two lateral fields centered on the cerebellum; and 5 months later, 800 r to the same fields.

Four months after the completion of this treatment, the patient appeared in the Medical Out-Patient Department of the Children's Hospital complaining of headache and vomiting, but the fact that she had been treated for a cerebellar tumor was not disclosed until her mother was questioned about the cause of the obvious alopecia. The signs at that time were characteristic of a cerebellar tumor; contact was made with the staff of the hospital where she was already under treatment, and she was returned to their care. Within a few days she received 800 r to the right and left cerebellar fields. A month later she received 600 r to the same fields and 600 r to the posterior cerebellar field. It was stated that "at first the patient responded rather well to the treatment, but after the last two series it appeared that she was becoming refractive, since there was little if any response; further treatment was therefore not given."

At the time of her last visit, the patient was found to have chronic papilledema, with secondary atrophy and distinct disturbance of co-ordination, so pronounced that she could hardly walk. She was given a very poor prognosis and told to return when necessary. A few days later, she was admitted to another hospital with the complaint of headache and vomiting. At this time, it was noticed that vision was very grossly impaired; the patient presented signs of high intracranial pressure, with cerebellar dysfunction. She was referred to the Children's Hospital, where she was admitted in a very poor condition, with very little vision remaining, and in almost complete prostration. A ventricular tap was done immediately after admission, and the fluid found to be under markedly increased pressure. Following this tap she improved considerably, and it was believed that she would tolerate a suboccipital exploration. This was carried out the day following admission, and a large cystic tumor was found extending into the mid-line from the left cerebellar hemisphere. The cyst contained clear amber fluid such as is usually found in an astrocytoma. The cyst wall was fixed with Zenker's solution after evacuation, and the solid portion of the tumor removed. The patient made a satisfactory but rather slow convalescence, and was discharged from the hospital about 6 weeks after admission.

The pathological report was as follows:

On gross examination the specimen consists of nine fragments of soft, friable, pale-yellow tissue of irregular

*From the Department of Surgery, Children's Hospital and Harvard Medical School.

†Neurosurgeon, Children's Hospital; instructor in surgery, Harvard Medical School.

‡Fellow in neurosurgery, Children's Hospital; assistant in surgery, Harvard Medical School.

shape, ranging from 5 to 10 mm. in average diameter. Formalin section, done on one fragment, shows tissue to be consistent with that of an astrocytoma. The material is fixed in Zenker's fluid and formalin.

Fifteen sections were made and stained with eosin and methylene blue, phosphotungstic acid and hematoxylin, and aniline blue. Microscopically, the greater part of the sections consist of well-preserved, fairly homogeneous, neoplastic tissue. The predominant cell is stellate, with a round or oval vesicular nucleus and a small, deeply basophilic nucleolus. Two or three delicate fibrillar processes extend from a scanty cytoplasm. In some places the processes terminate along walls of small blood vessels. These fibrils, together with coarser fibers, comprising a loose intercellular substance, stain blue with phosphotungstic acid and hematoxylin. No mitoses are seen. The cells do not form rosettes, palisades or other characteristic configurations. There is moderate vascularization of the tumor, with small areas of epithelial proliferation and calcification in some of the vessels. Small areas of recent hemorrhage are scattered throughout.

Diagnosis: fibrillary astrocytoma.

With this case history, we should like to present some of the data from our series of intracranial tumors, which suggest that it is impossible to make an accurate pathological diagnosis preoperatively, and that some of the prevalent ideas about intracranial tumors of children are incorrect.

TABLE 1. *Variation in Classification of 104 Consecutive Brain Tumors.*

DIAGNOSIS	NO. OF CASES
Pituitary adenoma	1
Unclassified glioma	1
Myxosarcoma of sphenoid bone	1
Astrocytic hamartoma of cerebrum	1
Lipoma of cerebrum	1
Fibrosarcoma of cerebrum	1
Hemangioma of cerebrum	1
Hemangioendothelioma of cerebrum	1
Neuroblastoma of cerebrum	1
Neuroblastoma of cerebellum	1
Neuroblastoma of 3rd ventricle	1
Teratoma of cerebrum	1
Teratoma of cerebellum	1
Ependymoma of all ventricles	1
Spongioblastoma multiforme of pons	1
Medulloblastoma of 4th ventricle	1
Ependymoblastoma of cerebrum	2
Medulloblastoma of 3rd ventricle	2
Astrocytoma of 4th ventricle	2
Ependymoma of cerebrum	3
Hemangioma of cortex	3
Spongioblastoma multiforme of cerebrum	3
Spongioblastoma multiforme of cerebellum	3
Astrocytoma of pons	4
Astrocytoma of 3rd ventricle	5
Ependymoma of 4th ventricle	6
Medulloblastoma of pons	7
Astrocytoma of cerebrum	8
Craniopharyngioma	9
Medulloblastoma of cerebellum	11
Astrocytoma of cerebellum	20
Total number of astrocytomas	39
Total number of medulloblastomas	21

In the first place, there is a general impression that medulloblastoma, which everyone agrees is radiosensitive and an almost hopeless surgical lesion, is the common intracranial tumor of childhood. In our series of 104 verified tumors (Table 1), there have been 21 children with medulloblastomas and 39 with astrocytomas. The patients were all under fifteen years of age. In the older age groups, the incidence of medulloblastomas falls off rather rapidly. For the age group in question, this difference is not unique. The figures are very similar in Bailey, Buchanan and Bucy's[2] series (30 astrocytomas, 13 medulloblastomas) and in Cushing's[3] series (40 astrocytomas, 24 medulloblastomas).

The other important phase of the question is an analysis of histories of these patients, particularly with regard to duration of symptoms.

Figure 1 presents a contrast between the history as originally presented and as interpreted after special study in each case. One pair of columns represents one patient, the solid column representing the real duration of symptoms, the broken one the duration as originally presented by the family. Obviously, the majority of patients with astrocytomas present histories of symptoms of longer duration than those with medulloblastomas. So far as any individual case is concerned, it is quite impossible to determine the pathological diagnosis preoperatively.

Another item of importance is that some patients, particularly children with cerebral tumors, present apparently unmistakable cerebellar signs: 12 of our patients with supratentorial lesions had predominantly cerebellar signs. This is not an unusually high percentage in this age group; this pitfall was described with numerous examples by Bailey[4] in 1924. Cushing[5] had a striking example of this source of confusion in a small child with a large craniopharyngioma; in this case, the cerebellar signs were so striking that the surgeon who had previously treated the patient had tapped the cyst through a cerebellar approach. Certainly these patients would not be improved by radiation of the whole central nervous system, which is the routine treatment for medulloblastoma.

We realize that when radiation is started in the presumed medulloblastomas the plan is not to continue it unless there is a favorable response clinically. The case reported above illustrates very well how impossible it is to judge by the apparent response to the first ten days' treatment whether the diagnosis is correct. The record states that "at first the patient responded rather well to the treatment, but after the last two series it appeared that she was becoming refractive." The improvement was presumably owing to the fact that the coronal suture had separated widely at about that time. Even without the separation of the sutures, it is not uncommon to have unexplained spontaneous remissions in an otherwise steadily progressive course. It is not at all clear how such remissions can be distinguished from the beneficial effect of x-ray treatment, and there is therefore no

justification for depending on this improvement for a verification of diagnosis.

In view of these several considerations, we consider a biopsy essential for an accurate diagnosis. Since a biopsy cannot be made safely without a decompression, a second important factor is taken care of — additional room, which should be provided if radiation is indicated when an accurate histologic diagnosis has been made.

We are not interested in emphasizing an error made by one surgeon or one clinic. As an advocate of this procedure has suggested, one mistake does not invalidate a method. This is certainly true, but the important point is that one cannot hope to have patients under better control or under more careful supervision than in the clinic where this patient was treated. Therefore, one must expect still more disastrous results when patients with suspected brain tumors are given a trial course of x-ray therapy in less central and less expertly controlled clinics.

It should also be noted that because of the local emphasis on this type of management medical students go through school with the impression that this procedure is generally accepted, whereas, actually, it is not generally accepted or approved throughout the United States.

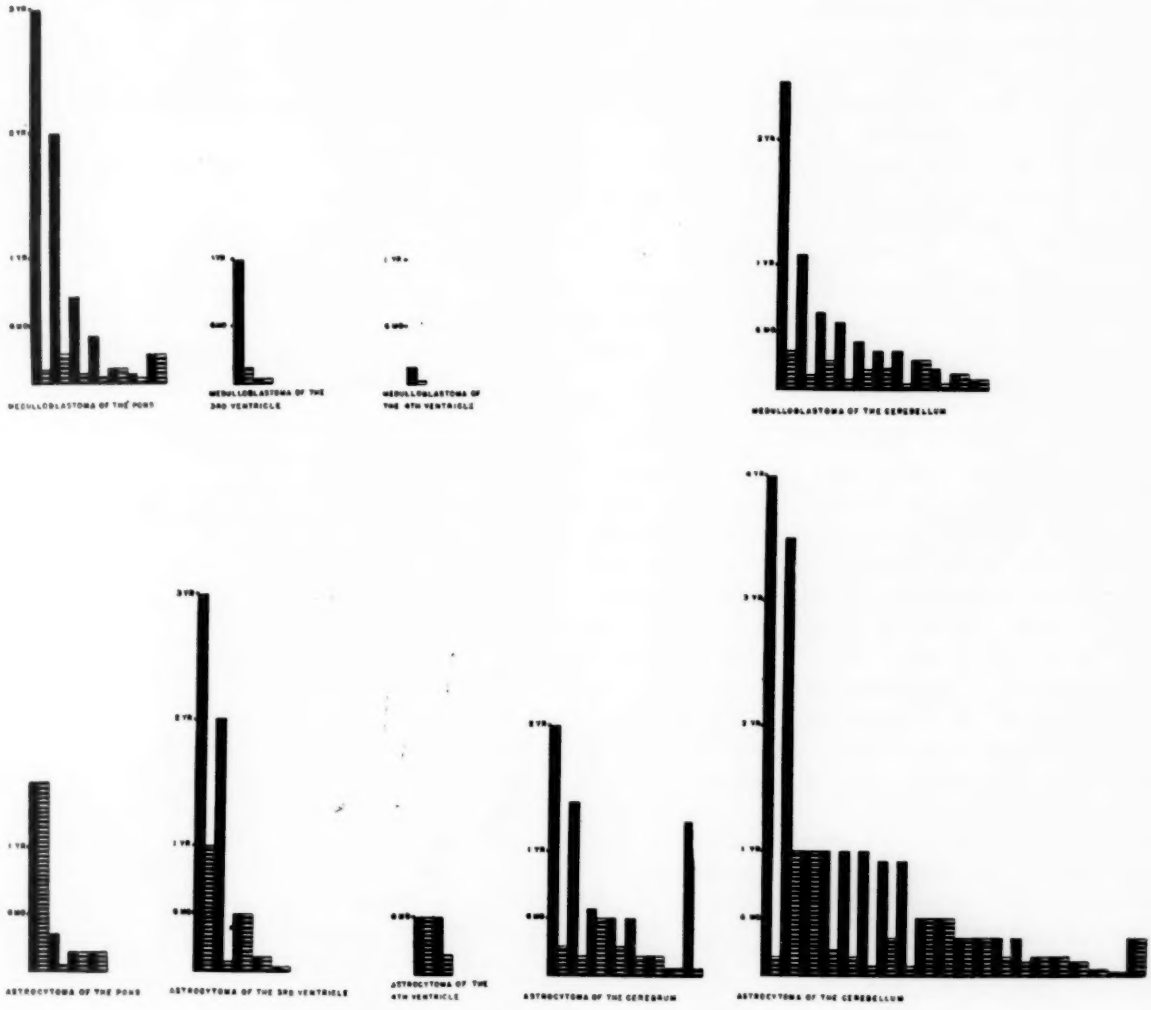

FIGURE 1. *Differences in the Reported and Actual Duration of Symptoms.*

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A STUDY OF THE SLIPPING-RIB-CARTILAGE SYNDROME*

JOHN F. HOLMES, M.D.†

MANCHESTER, NEW HAMPSHIRE

THE purpose of this paper is to call attention to an abnormal mobility and deformity of the anterior ends of the lower costal cartilages that cause painful symptoms, and to report cases observed over a period of twenty-seven years, emphasizing particularly persistent cases relieved by a simple operative procedure.

It should be understood that this particular syndrome has reference to the anterior ends of the rib cartilages and with the interchondral articulations, and is in no way concerned with the osteochondral junction of the anterior ends of the ribs, and that, barring anomalies, mistakes in numbering the ribs and exceptions, it has to do with the eighth, ninth and tenth rib cartilages only.

This symptom complex was first reported by Cyriax,[1] of London. He specifically mentions 3 cases, all treated expectantly. In 1922, Davies-Colley,[2] of London, under the original title, "Slipping Rib," reported 2 cases of displacement of the anterior end of the rib cartilage, which he had operated on by resection of the loosened cartilage with "complete relief of symptoms." From this time until 1924, 8 other cases by five authors[3-7] were reported in the *British Medical Journal*. In 1931, Bisgard,[8] of Chicago, referred to Davies-Colley's[2] article and other published cases, and reported 1 case, which he had operated on with cure. In the same year, Darby,[9] of Vancouver, Washington, referred to Bisgard's publication and described a typical case of slipping rib cartilage that was also operated on by resection of the cartilage and followed by relief of pain.

This makes a total of 15 cases reported from 1919 to 1931, 8 of which were operated on by resection of the cartilage, with complete relief of symptoms.

Davies-Colley noted:

> It is probably not a rare condition and is a trivial enough complaint in itself but it gives rise to most irksome symptoms. . . . In its [the pain's] position at the costal margin it resembles that due to so many deeper lesions of the abdomen and thorax, that I think it is quite likely that many cases occur in which such an apparently unimportant cause as a movable rib cartilage is unsuspected and the diagnosis missed.

Slipping rib cartilage is apparently of fairly common occurrence, and often produces irksome, incapacitating symptoms. It is diagnosed by physical examination, and cured by a simple operative procedure. As stated by Davies-Colley, "it is curious that it should receive no recognition in modern textbooks of surgery," and by Bisgard, "it has received but little attention in medical literature."

Because of failure to recognize this symptom syndrome, needless laparotomies have been performed, and prolonged suffering and incapacity from an easily curable condition are often permitted. Moreover, there does not appear to be any clear conception of the development of this deformity. These facts justify an attempt to secure a better understanding and more general recognition of this entity.

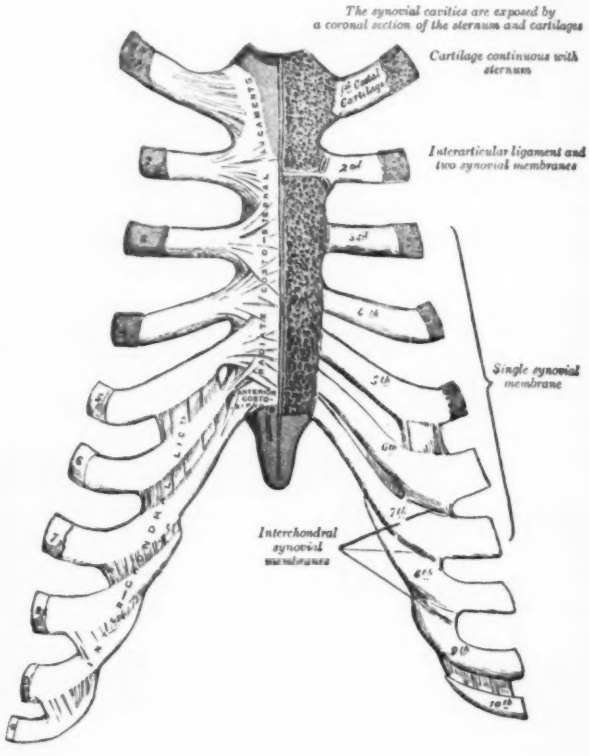
The synovial cavities are exposed by a coronal section of the sternum and cartilages
Cartilage continuous with sternum
Interarticular ligament and two synovial membranes
Single synovial membrane
Interchondral synovial membranes

FIGURE 1. *Sternocostal and Interchondral Articulations: Anterior view.*[11] *(Reproduced by permission of the publisher.)*

This loosening deformity involves the costochondral cartilages of the lower ribs, notably the eighth, ninth and tenth, either by displacement of fracture fragments or dislocation of the cartilage, or more often by curling of the end of the loosened

*One of the two essays awarded the Pray and Burnham prizes for 1940 by the trustees of the New Hampshire Medical Society.

†Surgeon, Elliot Hospital, Manchester, and Hillsborough General Hospital, Grasmere, New Hampshire.

cartilage, so that on respiration or motion the deformed end slips over or rubs against the inside of the rib above, with a click that is felt by the patient and, in some cases, with a severe and incapacitating pain.

Figure 1 shows the framework of the anterior chest wall; the anterior ends of the cartilages of the eighth, ninth and tenth ribs are usually attached to the one above, not by cartilaginous union, but by a fibrous hammock surrounding the interchondral synovial membranes of the interchondral articulations that lends to the desirable mobility of the anterior chest. At the same time, however, it has the instability characteristic of any joint, and hence the susceptibility to trauma.

Lilienthal[10] states that "the weakest part of the thorax is along the costochondral line on either side." This is an important observation in the consideration of cause and effect.

Etiology

Abnormal mobility of these rib-cartilage ends may begin acutely as a result of fracture or dislocation of the cartilage, or more often as a partial separation of the fibrous attachment. On the other hand, it may be the result of multiple injuries, which have stretched the fibrous attachments over a period of time — as from golfing or one-sided weight carrying. That trauma, direct or indirect, is the etiologic background seems reasonable.

Deformity of the loosened cartilage end may result from displacement of a fracture or dislocation, as will appear in one case reported, but is more often due to a curling upward of the loosened cartilage end — so that it rises above the contiguous rib cartilage, mechanically slipping out and in over the superior cartilage on certain movements of the chest or arms, or by digital manipulation, with a click and a pain that are diagnostic.

From a review of 33 cases, 15 reported and 18 of my own, it appears that slipping rib cartilage occurs more frequently from indirect than from direct trauma, there being 13 of the former and 6 of the latter; in 2 cases, both direct and indirect force were in evidence. Of the 12 other cases reported, no attempt was made to ascribe the cause, owing, I believe, to incomplete histories.

A sudden blow of the steering wheel of an automobile against the lower ribs is one method of direct injury. Indirectly it may be caused by sudden flexion, extension or twisting of the body; by repeated distortion of the body, as the one-sided weight carrying of an industrial worker; by a sudden pull on the arms, as in weight lifting or pushing; by repeated arm pulls, as in golfing; by forced compression or expansion of the chest, as in childbirth or coughing; and by many other types of force.

In his original report of this entity, Cyriax[1] said:

> Pain and tenderness produced by displacement of the anterior ends of the ribs or cartilages is doubtless due to irritation of the intercostal nerves in the vicinity, from which it may radiate to the posterior spinal nerves and thence to the thoracic or abdominal sympathetics.

Figure 2 shows the logic of this statement. According to Gray,[11] the intercostal nerves "pass forward in the intercostal spaces below the intercostal vessels." The description continues:

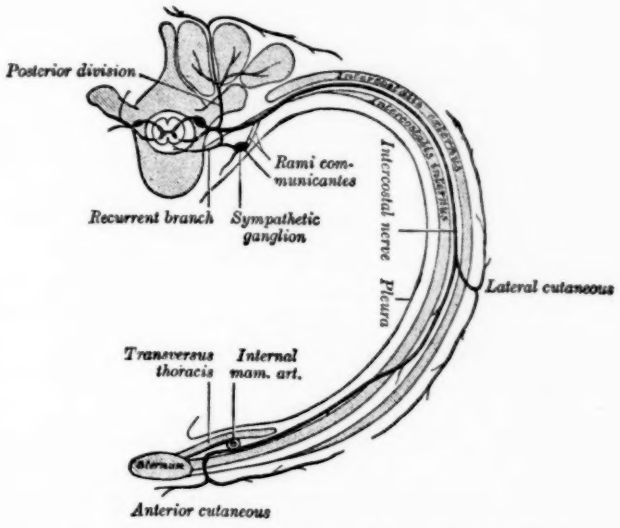

FIGURE 2. *Diagram of the Course and Branches of a Typical Intercostal Nerve.*[11] *(Reproduced by permission of the publisher.)*

> At the back of the chest they lie between the pleura and the posterior intercostal membranes but soon pierce the latter and run between these two planes of intercostal muscles as far as the middle of the rib. They then enter the substance of the Intercostalis interni and, running amidst their fibers as far as the costal cartilages, they gain the inner surface of the muscles and lie between them and the pleura. Near the sternum, they cross in front of the internal mammary artery and the Transversus thoracis muscle, pierce the Intercostales interni, the anterior intercostal membranes, and Pectoralis major, and supply the integument of the front of the thorax over the mamma, forming the anterior cutaneous branches of the thorax.
>
> Each nerve is connected with the adjoining ganglion of the sympathetic trunk by a gray and white ramus communicans.

Thus it is seen that the intercostal nerve lies very superficially on the inner surface of the anterior end of the rib and the rib cartilage, so that when the anterior end of the rib cartilage below becomes detached and deformed and slips up under the rib cartilage above, there is a strong

likelihood of nerve irritation. This probability is borne out by the fact that in every case reported, when the deformed cartilage is removed and clearance of the rib end established, the pain disappears immediately and permanently.

As cited by Cyriax,[1] and later by Davies-Colley,[2] the close association of the intercostal nerves with the sympathetic system accounts for frequent pain symptoms that suggest intra-abdominal or intrathoracic lesions, and has led to mistaken diagnosis.

Whether the synovial membranes of the interchondral joints that are involved in this slipping-rib-cartilage deformity contribute in any way to the pain manifested should be considered. So far, the pathological examinations of specimens obtained from these operations have revealed nothing of special interest.

Deformity of the loosened rib cartilage to produce the click and the accompanying pain develops secondarily, and hence may not be recognized as coming from the original injury. With this in mind, I believe a carefully taken history will, in all cases, show the original cause to be direct or indirect trauma.

Diagnosis

Diagnosis of slipping rib cartilage is made from the complaint of pain, usually in the rib border, and by digital examination, with the patient relaxed and supine, with the knees flexed, in which position the abnormally movable rib cartilage, with its associated click and pain, can be demonstrated. Limitation of chest expansion as demonstrated by measurement is a suggestive diagnostic feature.[1,2] It is of the greatest importance in diagnosis to have in mind the possibility of this entity and a clear understanding of its development.

Treatment

Treatment of these cases as reported in the literature has largely consisted in excision of the rib cartilage involved, and has been followed by immediate and complete relief of symptoms.

I have treated the acute condition conservatively by adhesive strapping. Some of my patients have, in part at least, recovered with conservative treatment. Some of them have tolerated the pain and have preferred not to be operated on. The 8 patients whose symptoms have persisted and who have submitted to operation have been treated by excision of the rib cartilage or cartilages involved, which has resulted without exception in immediate and permanent cure.

Before operating on these patients, I have advised a two-day skin preparation, preceded by one or two hot-tub soaks. At operation I select a point in the midaxillary line about three fingerbreadths above the umbilicus. With this point as a center, the incision is carried along and just above the rib border — 5 to 8 cm. Through the skin incision the operator's fingers are hooked under the rib border, and the offending cartilage is brought into the field. With the cartilage well supported by the fingers, a longitudinal incision is made through the muscles over the cartilage, exposing it. The soft tissues are pushed away, back to the junction of the rib, where the cartilage is disarticulated, and removed. It is quite brittle and may easily be broken in manipulation. This is an inconvenience and should be avoided. Careful digital examination, for abnormal mobility, is made of the adjacent cartilages. If any affected cartilage is found, it should be removed. In closure, the incised muscle is drawn in between the resected rib end and the rib above with plain catgut suture, and the end of the resected rib is buried in muscle. The skin is closed with interrupted sutures.

Operative Results

Of the 16 patients with slipping rib cartilage operated on, — 8 in the literature and 8 of my own, — 8 were women and 8 were men. The ages ranged from sixteen to fifty-seven years. The condition occurred on the left in 7 cases, on the right in 8 and once bilaterally.

One rib was involved in 12 cases, two ribs in 2 cases, three ribs in 1 case and four ribs in 1 case.

In all cases there was an area of tenderness at the site of the lesion. In some cases the pain was sharp and incapacitating at times, being aggravated by twisting or bending the body, by deep inspiration or by motion of the arms. It radiated, in a different manner in each case, along the costal and sternal margins, to the back and into the abdomen. The patients frequently had a sensation of something slipping or giving way at the costal margin, coincident with a click and a pain. Some patients had the sensation of a "bunch" at the rib border, associated with pain. In a favorable position the patients were usually comfortable, but pain could be produced at any time by motion of the body or by manipulation of the loosened cartilage, so that the subjects were in constant fear of pain.

Following excision of the offending rib cartilage or cartilages, immediate and permanent cure was obtained in every case.

Case Reports

Case 1. D. C., a 20-year-old woman, was first seen at the Elliot Hospital, Manchester, New Hampshire, on March 3, 1912. She stated that she had received a direct injury to her left rib border, the result of a fall 3 months

previously, at which time she had suffered considerable pain. The chief symptom was pain in the left rib border on standing erect and on bending or twisting the body. The pain was occasional, with a slipping sensation. When lying down, the patient was comfortable.

Physical examination showed a deformity of the anterior end of the 10th left rib and cartilage.

At operation, the anterior end of the 10th left rib was found to be fractured. The anterior fragment, with its cartilage, was curled up under the costal border in such a way that it caused friction. The deformed end and the cartilage of the 10th left rib were excised. Ten days later, the patient was discharged well.

Case 3. N. S., a 57-year-old laborer, was first seen on his admission to the Hillsborough General Hospital on May 22, 1934. The patient stated that his trouble had begun about 3 months previously, as a result of pulling on brush. He complained of pain and discomfort in the right rib border, particularly on trying to stand erect or on deep breathing.

The patient stood in a crouched position, his body bent forward and to the right. His general physical condition was good. There was localized tenderness, and a slipping sensation at the right rib border, associated with a click and manifestations of pain. This condition was diagnosed as fracture of the 8th, 9th and 10th rib cartilages, with deformity. X-ray examination of the chest was negative.

On May 26, at operation, the anterior ends of the 8th, 9th and 10th right rib cartilages were found loosened from their attachments and deformed. They were curled up under the rib borders and could be slipped back over the ribs above with a click. They were excised, and good clearance of the anterior rib ends was established.

The patient was immediately relieved. He made an uneventful recovery and was discharged on June 8.

In April, 1939, the patient reported that he had had no return of the pain in the right rib border. Examination showed the ends of the 8th, 9th and 10th right ribs to be smooth and nontender.

Case 4. R. C., a 19-year-old bookkeeper, was first seen at my office on July 21, 1937. She stated that on June 21, when she was riding in the back seat of an automobile, the car ran into a tree and turned over. The patient was thrown to the top of the machine, and then fell to the floor. She was taken to a hospital, where examination showed "pain on pressure over the lower ribs on both sides." After 5 days she returned home, but complained of pain in the costal borders on both sides, pain in the back and limitation of abduction of the left leg.

The general physical condition was good. The patient stood in a stooped position, and walked with some difficulty. At the costal borders on both sides there was marked tenderness, and on manipulation the anterior ends of the 8th and 9th rib cartilages on both sides were found to be loosened. When these cartilages were displaced forward, a click, associated with severe pain, could be demonstrated. The patient's abdomen was symmetrical. There was marked limitation of abduction of the left leg, and limitation of motion of the back.

On August 6, x-ray examination at the Elliot Hospital showed a fracture of the left pubic bone. The sternum and ribs were normal. On August 27, Dr. Ezra A. Jones applied a plaster jacket, immobilizing the pelvis and lower thorax.

While the patient wore the plaster cast, she made little complaint of pain in the rib borders, but when the cast was removed and the back brace fitted, she had incapacitating and unendurable pain in the rib borders.

On January 4, 1938, she was admitted to the Elliot Hospital wearing a back brace. She complained of pain in the rib borders on both sides, aggravated by motion.

The patient stood in a crouched position. On digital examination of the costal borders, movable cartilages were felt, which slipped over the rib margins with a click and associated pain. She was nervous and depressed.

At operation on January 7, the 8th and 9th costal cartilages on either side were found detached at their anterior ends. The loosened ends were curled up under the rib borders. When the ends of the cartilages were manipulated, they came down over the rib borders with a click. The cartilages of the 8th and 9th ribs on both sides were excised. The following day, the patient stated that the pain in the lower ribs was gone. On January 21, she could stand erect and breathe freely; she was relieved of the old rib pain and was discharged from the hospital.

In April, 1939, the patient reported that, so far as her lower rib borders were concerned, she had no discomfort.

Case 5. L. L., a 55-year-old teamster and woodchopper, was first seen at my office, on January 1, 1939. He stated that on December 31, 1937, while driving in a light wagon, he was run into by an automobile, and was thrown out onto the frozen ground, falling on his head and right shoulder. His shoulder was bruised, and his back was painful. On reaching home he found that he could not sit or stand erect. When he bent forward and inclined to the left, he was fairly comfortable, but when he stood erect, he felt a sharp pain at the center of his back, at about the level of the costal border, and along the left costal border. His chest and back were strapped, and he received medical treatment for 5 or 6 weeks. After 8 weeks, he returned to work but found that he could not load logs, which necessitated raising his arms high and brought his body into an extended position, causing severe pain. Two weeks later, he went to work as a chopper, and although he had some pain, he could work in a crouched position. He complained of severe pain in the back, about the level of the 12th thoracic vertebra and along the left costal border, particularly on deep breathing and when he tried to stand erect.

His general physical condition was good. Chest measurements were as follows: in repose, 37¼ inches; on expiration, 37 inches; and on inspiration, 38 inches. The patient stood and sat in a crouched position, with an inclination to the left. There was definite tenderness in the left lumbar region, with limitation of back motion in all directions, lateral motion to the right being most marked. The diagnosis was dislocation of the 12th left rib, or fracture of the transverse process of the 12th thoracic vertebra, and injury to the left chest.

X-ray examination of the dorsolumbar spine and lower ribs showed a moderate degree of arthritic change in the spine, but no evidence of other disease. Adhesive strapping was applied to the left chest.

On March 8, further examination showed that there was a slipping 9th left rib cartilage, which on motion caused a click and a pain.

On May 2, at the Elliot Hospital, an operation was performed. The 9th left rib cartilage was found detached from the rib above and curled up in the form of a hawk's bill, the anterior end of the cartilage resting on the inside of the rib above, so that when manipulated, the curled end of the rib cartilage came out over the rib above with a click. The deformed 9th left rib cartilage was excised. The

following day the pain was gone, and on May 8, the patient was discharged from the hospital. In January, 1940, the patient stated that he had had no return of pain. He was comfortable and working regularly.

Case 8. W. M., a 29-year-old cutter setter, was first seen at my office on October 14, 1939, at the request of Dr. Philip McQuesten, of Nashua. The patient stated that on November 8, 1938, he was lifting a heavy box from about a foot above the ground, and as he raised it to the level of his shoulder, he felt a sharp pain in the right rib border. He dropped the box and sat down. He could not breathe. Dr. McQuesten, who attended him, strapped his chest. He gradually got over the sharp pain, but was unable to return to his work. He complained of pain in the right rib border, inability to use his hands and arms because of pain, and attacks of nausea.

His general physical condition was good. At the right costal border, there was a definite point of tenderness near the anterior end of the 8th rib cartilage. The cartilage was movable, and with considerable difficulty, a click, associated with pain, could be demonstrated. The diagnosis was slipping rib cartilage of the 8th right rib.

On November 21, an operation was performed at the Memorial Hospital, Nashua. Examination at the time of operation showed the 8th right rib cartilage to be loose and slipping, and a click could be demonstrated. The loosened cartilage was excised.

Dr. McQuesten reported that the patient made an uneventful recovery and returned to his work in about 5 weeks.*

Summary and Conclusions

Slipping rib cartilage is an entity presenting a classic clinical picture. It is trivial enough in itself, but often produces irksome and incapacitating symptoms.

The anterior ends of the eighth, ninth, and tenth rib cartilages and their interchondral articulations are the points involved.

It has no predilection for age or sex, but occurs most commonly in the ages of greatest activity and liability to trauma. It is usually confined to one side and one rib cartilage, but both sides and multiple one-sided lesions may obtain.

It is reasonable to suppose that trauma, direct or indirect, forms the etiologic background. Deformity of the movable rib cartilage, with its associated click and pain, seldom occurs at the time of injury, but develops later — hence the confusion in diagnosis.

This entity is easily diagnosed by the symptoms of pain in the rib border and by digital examination, with the patient in supine position and the knees flexed, when a movable rib cartilage, associated with a click and a pain, can be demonstrated. Limitation of chest expansion, as demonstrated by measurement, is a suggestive diagnostic feature. It is of the greatest importance in diagnosis to have this entity in mind and to understand its development. It is unwise to make a diagnosis of slipping rib cartilage at the time of an acute injury.

Slipping rib cartilage does not always cause pain, or pain at all times.

Slipping rib cartilage may be relieved by conservative treatment. Patients may prefer to tolerate the pain and not be operated on. In the persistent incapacitated cases, excision of the loose cartilage or cartilages should be performed, and will result in complete and permanent cure.

The pain symptoms at the costal margin resemble those of so many deeper lesions of the abdomen and thorax that it is probable that many cases occur in which such an unimportant cause as movable rib cartilage is unsuspected, and the diagnosis missed.

A better understanding and a more general recognition of this entity are desirable.†

*Cases 2, 6 and 7, which were operated on and which appear in the Pray–Burnham Prize Essay, are omitted to avoid repetition of points covered in other cases. The cases of 10 patients not operated on, which were also reported, are omitted for brevity.

†Since writing this essay I have operated on 7 other patients. I am also privileged to report 5 other cases that have been operated on: Dr. W. J. P. Dye, Wolfeboro, New Hampshire, 1 case; Dr. Clarence Butterfield, Concord, New Hampshire, 1 case; Dr. Howard K. Gray, Rochester, Minnesota, 3 cases.

814 Elm Street

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THE PROLONGED USE OF ENTERIC-COATED TABLETS OF THEOBROMINE SODIUM ACETATE IN THE TREATMENT OF EDEMA AND ANGINA PECTORIS*

JOSEPH E. F. RISEMAN, M.D.,† AND HARRY LINENTHAL, M.D.‡

BOSTON

THE use of xanthines in the treatment of edema has decreased greatly since the introduction of mercurial diuretics. The comparative popularity of mercurials is due not only to their superior diuretic action but also to the absence of the severe gastric distress that frequently attends the use of theobromine and theophylline derivatives. The mercurial diuretics possess disadvantages, however; they must be given intravenously, intramuscularly or rectally, great care must be exercised to prevent sloughing or thrombosis, and their administration to patients with renal damage is not without danger. There are therefore many cases in which an effective oral diuretic would be of value either as an adjunct or in place of a mercurial diuretic.

Theobromine and theophylline sodium acetate have been shown to be efficient xanthines in the treatment of angina pectoris.[1, 2] All xanthines, however, cause nausea and heartburn when given in large doses.[2] The following case histories illustrate that these untoward gastric effects may be minimized by encasing the medication in a so-called "enteric coating," thus often permitting its prolonged use in amounts adequate to keep certain patients free from edema.

CASE REPORTS

CASE 1. N. G., a 66-year-old man, with chronic suppurative pulmonary infection and frequent acute febrile episodes for over 30 years, showed fibrosis of the left lung, with traction of the mediastinum to that side. In 1923, he retired from active business. Hypertension was first noted in 1924; one year later, left nephrectomy was necessary because of renal calculi. Pathological examination of the removed kidney revealed "subacute interstitial nephritis." After 1930, he had numerous episodes of paroxysmal auricular fibrillation that were relieved by quinidine and digitalis. In 1934, the urine began to show moderately large traces of albumin and a relatively fixed specific gravity; thereafter the blood pressure ranged between 200/100 and 250/150. In 1935, a right hemiplegia was followed by almost complete recovery.

In November, 1937, peripheral edema and an enlarged tender liver were noted for the first time. The electrocardiogram showed marked left-axis deviation, with notched QRS waves in Leads 1 and 4 and inversion of the T waves in those leads. The nonprotein nitrogen of the blood was 44 mg. per 100 cc.

Because of the renal lesion, it was inadvisable to restrict the fluid intake to less than 2000 cc. The edema failed to disappear, and the patient became drowsy and irritable. Aminophyllin (0.2 gm. three times a day) and later theophylline calcium salicylate (0.26 gm. three times daily) produced a satisfactory diuresis and a loss of all visible edema in 3 to 5 days. The patient became so nauseated, however, that it was necessary to discontinue the therapy, and the edema returned promptly. The administration of smaller doses was followed by the same gastric distress and a lessened diuretic effect. A commercially available enteric-coated aminophyllin tablet (Byk) and also tablets of theophylline calcium salicylate coated with salol were used with the same results. Although potassium chloride was of some value, the patient could tolerate only approximately 0.5 gm. a day, and the edema did not disappear entirely. Mercurin rectal suppositories were tried on two occasions but caused local irritation and little diuresis. Intravenous mercurials were avoided because of the evidence of damage in the remaining kidney.

About 8 weeks after the onset of the edema, intravenous aminophyllin (0.25 gm. in 10 cc.) was given every other day. Marked diuresis and loss of about 8 pounds resulted, but within 48 hours the swelling of the dependent parts regularly returned. After 3 weeks the dose had to be increased to produce diuresis; within 2 months the patient was receiving 1.0 gm. (40 cc.) of aminophyllin intravenously every other day; each dose was followed by diuresis and a loss of 3 to 5 pounds of weight, but in the course of the next 24 to 48 hours, the edema always reappeared and was associated with drowsiness and mental confusion. At no time did the intravenous xanthines cause gastric or cerebral irritation.

The effectiveness of aminophyllin intravenously suggested that if a drug of the xanthine series could be given by mouth without producing nausea, the necessity for repeated intravenous injections might be obviated. The problem was presented to several pharmaceutical houses. Several enteric coatings were prepared and tested, not only for their solubility in acid and alkaline solutions, but also for their value as a coating for theobromine sodium acetate when given to patients with angina pectoris. In March, 1938, a tablet of theobromine sodium acetate, enteric coated with cetyl alcohol, was made available and appeared to have the desired physical and clinical properties. Roentgenograms were taken after administering by mouth tablets of barium sulfate coated with cetyl alcohol. The tablets passed through the stomach intact and disintegrated in the small intestine. With catharsis or diarrhea, the tablets passed through the intestinal tract intact. From four to eight 0.5 gm. tablets of theobromine sodium acetate, enteric coated in this manner, were administered to patients with angina pectoris and normal laboratory workers in

*From the Medical Research Laboratories and the Medical Service, Beth Israel Hospital, the Department of Medicine, Harvard Medical School, and the Department of Medicine, Tufts College Medical School.

†Instructor in medicine, Harvard Medical School; associate visiting physician and associate in research, Beth Israel Hospital.

‡Professor of clinical medicine, Tufts College Medical School; physician-in-chief, Beth Israel Hospital.

single doses without gastric distress, and with no demonstrable weight loss or diuresis.

On the basis of these findings, the patient was given the enteric-coated tablets of theobromine sodium acetate by mouth in doses of 0.5 gm. three times daily. Four hours after the first tablet was given, diuresis began; after approximately 10 days, all visible edema had disappeared, the patient became mentally clear and less drowsy and no further intravenous medication was needed. From the onset of this medication until death 3 months later, the patient was free of visible edema, with the exception of one experimental period when the medication was stopped for a few days and the edema promptly returned. Death was due to an exacerbation of the pulmonary condition, with fever, and uremic coma.

Comment. This patient with chronic suppurative pulmonary disease, hypertension and congestive heart failure, had nephritis of the one remaining kidney. The administration of a diuretic by mouth was indicated, but the available preparations caused marked gastric distress. An enteric-coated tablet of theobromine sodium acetate was developed and tested both in the laboratory and on patients. From the time this preparation was first administered to the time of death no additional diuretic therapy was necessary.

Case 2. Mrs. R. H., a 63-year-old woman, had a cerebrovascular accident in 1930, followed 3 months later by myocardial infarction. She recovered from both episodes and, despite the onset of auricular fibrillation in 1931, was able to carry on her household duties for over 6 years. Late in December, 1938, she was sent to the Beth Israel Hospital because of dyspnea on exertion, easy fatigability and dependent edema, all of 15 months' duration. For several weeks she had experienced attacks of paroxysmal nocturnal dyspnea, and for about 1 week had had considerable nausea and vomiting.

Physical examination showed moderate cardiac enlargement, a rough apical systolic murmur, completely irregular rhythm, a blood pressure of 210/110, a tender liver edge at the level of the umbilicus, rales at both bases of the lungs, signs of free fluid in the right chest cavity and pitting edema of moderate degree up to the knees. Laboratory data, including urine examination, blood counts and smears, blood nonprotein nitrogen, serum icterus index and blood serological tests, revealed no relevant facts. The electrocardiogram showed auricular fibrillation and depression of the ST segments in Leads 1 and 2, with partial inversion of the T waves in all leads.

During 38 days in the hospital the blood pressure fell to 160/90, and the signs and symptoms of congestive failure diminished markedly. The maintenance dose of digitalis was found to be 0.2 to 0.3 gm. daily. On the 4th day 750 cc. of fluid was removed from the right chest. Neither aminophyllin intravenously nor potassium chloride by mouth was of value as a diuretic. A mercurial diuretic (Mercupurin, 2 cc.) was administered intravenously on four occasions and by rectal suppository six times. Each treatment was followed by an increase in the urinary output from 500 to 1500 cc. and an improvement in comfort; however, pitting edema, rales and dyspnea became evident again within a few days.

Following discharge it was necessary to administer mercurial diuretics intravenously every 5 to 7 days. Late in March, 1939, enteric-coated theobromine sodium acetate therapy was begun (0.5 gm. four times daily). For the next 4 weeks no additional diuretics were necessary, and the patient remained free of edema. Her family physician then discontinued the xanthine therapy and resorted to intravenous diuretics, but the signs and symptoms of congestive failure returned. When enteric-coated tablets of theobromine sodium acetate were again administered, intravenous mercurials became necessary only about once in 4 or 5 weeks. Three months later the patient died, a few days after another cerebrovascular accident.

Comment. This patient with arteriosclerotic heart disease, auricular fibrillation and congestive failure required intravenous mercurial diuretics every 6 to 7 days. Following the administration of enteric-coated tablets of theobromine sodium acetate, the intravenous therapy was unnecessary for weeks at a time. Cessation of the xanthine therapy resulted in reappearance of the signs and symptoms of congestive failure, only to be favorably affected by readministration of the drug.

Case 3. N. B., a 51-year-old tailor with mild diabetes mellitus, had suffered from attacks of substernal and precordial pain that occurred on the slightest exertion or emotion from two to eight times daily and usually lasted "2 minutes." These attacks were relieved by rest and nitroglycerin and were more frequent during the winter. He had been confined to bed for several weeks on three occasions because of prolonged attacks.

Examination showed a short, stocky and exceedingly apprehensive man. There were peripheral and retinal arteriosclerosis and pulmonary emphysema; the blood pressure was 130/85. An electrocardiogram and a 7-foot x-ray plate of the heart were normal.

When first seen in the clinic on November 4, 1938, the patient was receiving digitalis and was complaining of constant oppression, relieved slightly by nitroglycerin. Digitalis was omitted after 1 month of observation; the constant pain disappeared, but he experienced four to eight attacks daily. During the course of the next 16 months, eight different medicinal therapeutic measures were used, but none were effective except theobromine sodium acetate (0.5 gm.) and quinidine sulfate (0.3 gm.), which resulted in moderate improvement clinically (one to three attacks a day) and a slight increase in exercise tolerance, as measured under standardized conditions. On May 4, 1940, enteric-coated theobromine sodium acetate (1.0 gm. four times daily) was prescribed, with an additional dose (0.5 gm.) of the uncoated medication in the morning. On this regime the patient could walk farther, and the attacks were less numerous (two to three a week); the exercise tolerance increased. Each time tablets of lactose or sodium bicarbonate of similar appearance were administered, he again experienced eight to ten attacks daily, and his exercise tolerance decreased. Each time 1 gm. of theobromine sodium acetate was administered, four times daily, definite improvement resulted. Larger doses (2 gm. four times daily) resulted in nausea and diarrhea and made it necessary to decrease the dosage of the drug.

Advantages of Xanthine Therapy

These cases illustrate the effectiveness of diuretics given orally in treating cardiac or renal edema. This concept is not novel, but the method has not been of maximum practical value because of the frequency of nausea and heartburn following their ingestion in adequate doses. During the last two years several effective enteric-coated preparations of theobromine and theophylline sodium acetate have become available commercially, and it is no longer necessary to rely on chemical houses

for a special supply of these drugs. In our experience the enteric-coated theobromine sodium acetate marketed by Brewer and Company, Incorporated, and by E. R. Squibb and Sons and the theophylline sodium acetate marketed by the Upjohn Company, although covered with different enteric coatings, are effective diuretics that can be given by mouth in adequate dosage (one tablet four times daily) over long periods without gastric distress. We have found them of value in cardiac edema both with and without valvular damage or abnormal rhythm, and irrespective of whether the heart disease is of rheumatic, hypertensive or arteriosclerotic origin. We have had no experience with their use in syphilitic heart dsease or cor pulmonale. Their greatest value has been in patients who required frequently repeated intravenous injections of mercurial diuretics. In such cases intravenous therapy was frequently unnecessary. Not all patients respond to this therapy, but the advantages of administering the xanthines by mouth make a trial advisable.

Disadvantages of Xanthine Therapy

The enteric-coated tablets are not so effective as the intravenous mercurials for the removal of accumulations of large amounts of edema fluid. Doses of 2 to 3 gm. of theobromine sodium acetate have been administered four times daily for two or three days to several patients with marked edema. Although these doses were usually well tolerated, the diuretic response was not satisfactory, and the intravenous mercurials had to be invoked to eliminate the residual edema.

It has been suggested that the gastric distress which may follow the use of the xanthines is due mainly to a central rather than a local action. This does not seem to be true, for patients who cannot tolerate small doses of the uncoated drug by mouth may take large doses of the enteric-coated tablets orally without distress and with excellent therapeutic response; furthermore, large doses of aminophyllin can be given intravenously without gastric distress (Case 1).

The possibility of cerebral stimulation following the prolonged use of the xanthines has been another objection to their use. The close chemical relation of theobromine and theophylline to caffeine is probably responsible for this concept. We have administered 0.5 gm. of the enteric-coated theobromine sodium acetate 4 times a day for months to more than 100 patients with angina pectoris without observing a single case of nervousness, irritability or sleeplessness or any other evidence of cerebral irritation or stimulation.

Use in Angina Pectoris

Not all patients with angina pectoris respond to the sodium acetate derivatives of theobromine or theophylline, but it is apparent that they are of value in approximately half the cases. That the effect of the medication is not entirely psychologic is shown by the increased amount of work that patients can do after the administration of the drug, and also by the fact that these drugs prevent the electrocardiographic changes that would otherwise occur during exertion.[3]

Adequate dosage is of the utmost importance. Unless the purines are given frequently in sufficiently large amounts and over long periods, the optimum therapeutic results will not be obtained. It has been found that the optimum dosage is usually the maximum amount that can be administered without inducing nausea.[2] The dose that has been found to be satisfactory for most patients was 0.5 gm. of theobromine sodium acetate or 0.2 gm. of theophylline sodium acetate given four times daily — before meals and before retiring. Most patients fail to derive benefit from smaller amounts. An occasional patient who does not respond to the usual dose may derive benefit from two or even three times this dose (Case 3). Some patients find the tablet of theobromine sodium acetate too large to swallow with ease, and a few experience slight gastric distress despite the enteric coating. In such cases it is advisable to give the medication more frequently but in smaller amounts (0.25 gm. five or six times daily).

The enteric coating delays absorption for four to six hours. It is obvious, therefore, that it is the medication taken before retiring that is effective in the early morning, and that a dose taken on arising may be of no value in preventing attacks of angina pectoris during the forenoon. Some patients continue to have pain during the morning despite this late evening dose. In such cases the administration of 0.25 or 0.5 gm. of uncoated theobromine sodium acetate on arising, in addition to the coated tablet, is of value. If the patient is free of pain during sleep, the dose after supper may be omitted.

So far as we know, the medication must be continued indefinitely in most cases, and any interruption of medication will usually be followed by a return of symptoms within a few weeks. An occasional patient, however, may be free from pain for several months after taking the medication for a few weeks. There is little evidence of development of a tolerance to the drug. Occasionally the use of the medication is followed by a period of freedom from pain, with later reappearance of discomfort despite continuation of medication. In

some cases, evidence of progression of the disease may be found, such as electrocardiographic changes and increased sedimentation rate.

Use in Other Cardiac Conditions

The success achieved with the use of theobromine sodium acetate in angina pectoris and edema has led us to employ the drug in other conditions, especially arteriosclerotic heart disease and hypertension, for according to recent investigations,[3] the drug causes coronary dilatation, and therefore better myocardial nutrition. We have never observed any appreciable lowering of the blood pressure following this medication. Some patients with cardiac asthma, however, appeared to have less frequent attacks following administration of the drug.

Conclusions

Enteric-coated tablets of theobromine sodium acetate and theophylline sodium acetate are now available, which make it possible to give therapeutically adequate doses of these drugs over long periods. By this means, the necessity of intravenous administration of diuretics may be obviated or decreased in certain patients with heart disease or nephritis, and the frequency and severity of attacks of angina pectoris may be diminished. When the drugs have been given continuously for a long time, no untoward effects have been observed except for occasional slight gastric discomfort. The optimum dosage for most patients appears to be 0.5 gm. of enteric-coated theobromine sodium acetate, or 0.2 gm. of enteric-coated theophylline sodium acetate, given four times daily, before meals and before retiring. Adequate dosage is necessary; in angina pectoris it is especially important to administer a dose of the medication before retiring.

45 Bay State Road

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DIAPHRAGMATIC ABNORMALITIES SECONDARY TO TUMORS*

A Roentgenologic Study

John W. Turner, M.D.†

SPRINGFIELD, MASSACHUSETTS

THE exact status of the diaphragm in non-neoplastic diseases is often difficult to determine from the clinical findings alone. In recent years, various x-ray diagnostic procedures have provided helpful supplementary evidence. Since the symptoms produced by most diaphragmatic abnormalities are difficult to interpret, it is not surprising that these conditions may be easily overlooked among patients with malignant tumors and that, consequently, many complaints are dismissed on the basis of probable visceral metastases or the patient's poor general condition. Thorough investigation both by x-ray films and fluoroscopy is essential for the recognition of most diaphragmatic disorders. Thus it seems highly desirable to direct more attention to patients with tumors who present symptoms referable to the diaphragm.

In recent reviews and reports of primary diaphragmatic tumors,[1-3] malignant neoplasms are about twice as common as benign ones. Much more frequently, the diaphragm is secondarily involved by metastases or by direct extension of a cancer primarily situated in the breast, lung, stomach or more remote organs. Most cases of secondary neoplastic invasion of the muscular structure of the diaphragm produce no striking symptoms, and attention is usually drawn to the site of the primary or of the skeletal and visceral metastases.

Moreover, changes in and adjacent to the diaphragm are not infrequent in patients with neoplastic disease — in addition to the primary and secondary diaphragmatic neoplasms mentioned above. Three separate entities seem worthy of further attention and are exemplified by the accompanying case reports.

Subphrenic Abscess

Perforation of a tumor of the colon has been listed by Graham[4] as an occasional cause of left subphrenic abscess, the more frequent causes being perforated peptic ulcer, post-partum infection, and the other conditions that produce a peritonitis. Although subphrenic abscesses are only 20 to

*From the Cancer Section, Westfield State Sanatorium, Massachusetts Department of Public Health.

†Radiologist, Westfield State Sanatorium; out-patient roentgenologist, Springfield Hospital.

25 per cent as common on the left as on the right in the average surgical practice,[5] among tumor patients the opposite distribution seems to hold, with neoplastic perforation as the most frequent cause. The stomach seems fully as important a site for neoplastic perforation as the colon.

It has often been found that the appearance of an unexplained pleural effusion, with pleural thickening and suppurative pneumonitis, may provide a helpful clue to possible subphrenic disease. Pleural and pneumonic complications from subphrenic

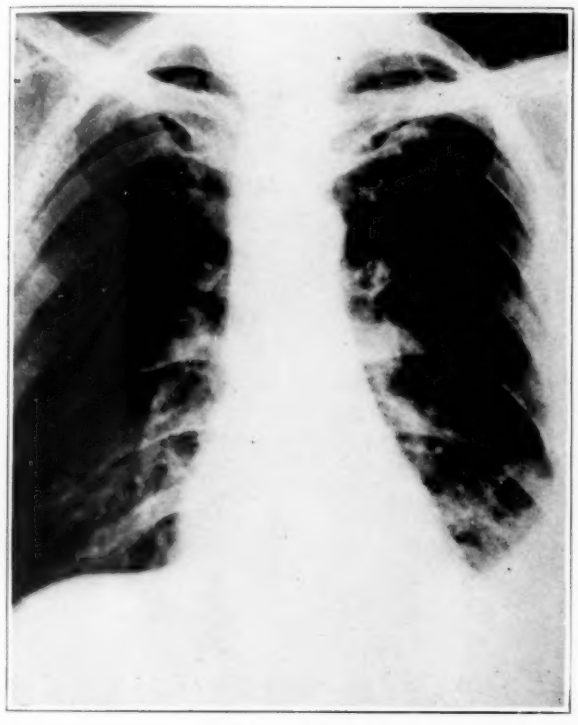

FIGURE 1. *Case 1.*

A routine chest film showing left basilar effusion and pneumonitis.

intraperitoneal abscess, which occur in 22 to 50 per cent,[6, 7] and from extraperitoneal subphrenic suppuration of perirenal origin, which occur in 16.5 per cent,[8] have been explained by the richness of the lymphatic supply, including extensive transphrenic communications. With fluoroscopic evidence of fixation of the affected dome of the diaphragm and the opportunity to visualize the barium-filled cardia of the stomach, early detection of subphrenic abscess is more certain. As compared with the same condition in patients without cancer, a contrast exists in the usually less severe illness seen in subphrenic abscesses that follow the slow perforation of a tumor, for the neoplastic tissue often contributes to the walling-off process. Maintenance of communication of the abscess cavity and a hollow viscus through the perforation, may also lessen the severity of the process by simulating the effect of drainage. It seems evident that the neoplasms that are well differentiated and show less frequent ulceration are the least likely to result in perforation. Among the tumors that increase the probability of this occurrence, the lymphoma group must be included.

CASE 1. A 48-year-old undertaker entered with complaints of tiredness and abdominal pains for the previous 6 months. The pain was described as sharp epigastric discomfort with radiation to the left costal margin. A Sippy diet had been tried, with the result that the character of the pain changed only from sharp to dull. There had been a weight loss of 76 pounds. A productive cough had been present for 4 weeks.

A roentgenogram of the thorax (Fig. 1) revealed marked left basilar pleuritis and evidence of fluid accumulation. Barium examination of the upper gastrointestinal tract revealed a very large ulcer crater involving the proximal portion of the greater curvature of the stomach (Fig. 2). The barium flowed readily from the

FIGURE 2. *Case 1.*

A film showing an irregular carcinomatous ulcer of the proximal greater curvature of the stomach, with escape of barium into a subphrenic abscess.

depth of the ulcer crater into a large subphrenic abscess cavity. After a few weeks of supportive treatment the patient expired as a result of a carcinomatosis.

Comment. This case presented a characteristic clinical picture of ulcerating carcinomatous involvement of the proximal greater curvature. The passage of barium from the stomach into the abscess cavity added convincing evidence of the mechanism involved in arriving at the end result of basilar pleuritis, effusion and pneumonitis.

Phrenic Paralysis

The reported causes of spontaneous phrenic paralysis are numerous, including compression by new growths and other masses, syphilis, diphtheria, scarlet fever, infantile paralysis, ascending paralysis and extensive mediastinal, basilar or generalized pleuritis.[9] However, this complication is relatively infrequent among patients in a general hospital. On the other hand, among tumor patients neoplastic phrenic paralysis is more frequent than all other causes combined. The variation in the level of the diaphragmatic domes in normal persons is so great that by x-ray evidence alone the condition may remain unrecognized unless fluoroscopic observation for paradoxical excursion is conducted.

The presence of phrenic-nerve invasion by neoplastic tissue is observed with or without other intrathoracic disease; thus, from a carcinoma of the breast, or any other cancer causing extensive neoplastic lower cervical and medial supraclavicular nodes, one may see phrenic interruption, even in the absence of pulmonary or mediastinal metastases. Occasionally both the phrenic and recurrent laryngeal nerves are invaded, with paralysis of the vocal cord and the dome of the diaphragm on the same side as the mass of palpable medial supraclavicular and cervical nodes. Occasionally the phrenic nerve is invaded as it passes through the superior mediastinum,[10] or along the middle mediastinum anterior to the hilar structures on each side or more distally between the pleura and pericardium. Thus it seems worth while to investigate any unexplained elevation of a diaphragmatic dome in a patient with cancer of the lung. One may assume that paralysis, if present, proves that a primary lung tumor has advanced beyond successful treatment by pneumonectomy, even though film evidence of such spread is lacking.

The return of function that occurs in cranial and other nerves after regression of the neoplasm from radiation therapy[11] also follows palliative application of x-ray for phrenic palsy. Frequently the dyspnea is quite distressing, even in the absence of any pulmonary involvement. It is surprising that return of motor function can occur in only a few weeks following radiation therapy. A recent case of sudden complete paralysis of the right sixth cranial nerve in a patient with widespread Hodgkin's disease disappeared in sixteen days after the first x-ray treatment. This was interpreted as indicating a compression of medullated fibers by neoplastic cells, rather than a complete division of such fibers by the neoplasm.

Case 2. A 34-year-old paper-mill employee was admitted with complaints of dyspnea, cough, fatigue and weight loss of 8 months' duration. Examination, which included x-ray studies and bronchoscopy, revealed a carcinoma simplex of bronchiogenic origin in the right lower lobe. A moderate elevation of the right dome of the diaphragm observed in the films (Fig. 3) was found on fluoroscopic study to be the result of complete phrenic-nerve paralysis. Hilar, mediastinal and supraclavicular nodes were enlarged. Palliative x-ray therapy caused regression of the thoracic disease, but there was a rapid decline in the patient's general condition, with terminal jaundice. At the last admission 3 months later, the icterus index was 90, and the serum van den Bergh revealed 10 mg. of bilirubin per 100 cc., direct reaction.

Post-mortem examination showed invasion of the right phrenic nerve from the medial right supraclavicular

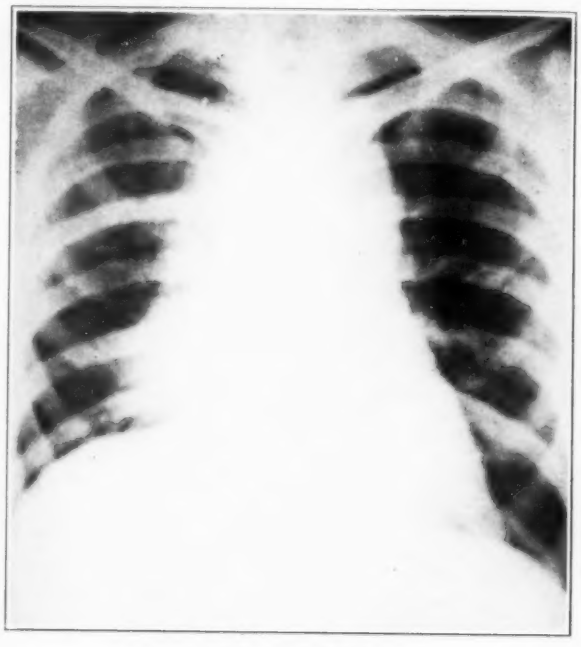

Figure 3. *Case 2.*

A film showing elevation of the right dome of diaphragm from paralysis, intrathoracic changes from a carcinoma of the right lower lobe and metastases to the right hilus and mediastinum.

metastatic adenopathy. Pancreatic metastases caused obstruction to the bile duct. Metastases to the heart, duodenum, mesentery of small bowel, adrenal glands, kidneys, cerebrum, and cervical, mediastinal, abdominal and pelvic lymph nodes were observed.

Comment. In this case there was obvious post-mortem evidence of phrenic-nerve invasion. The site of invasion was in the medial supraclavicular region, rather than at a more distal level. Thus the absence of a pulmonary lesion, as in cancer of the breast, does not exclude the possibility of phrenic palsy. In fact, phrenic-nerve invasion by neoplastic tissue seems more frequent at the level of the medial supraclavicular lymph nodes than any other section. Although treatment did not accomplish regression with return of function, such an occurrence has been observed in other cases.

Hiatus Hernia

As an occasional complication of large tumor masses or large accumulations of fluid within the abdomen, the formation of an epiphrenic gastric pouch by hiatus herniation deserves mention. Dur-

ing recent years symptoms referable to small gastric pouches above the diaphragm have received considerable attention and careful study. Evans and Bouslog[12] have reported its occurrence in pregnancy as a cause of pyrosis. Reid[13] has reported simulation of cardiac infarction by hiatus herniation, and a peptic ulcer in the lower esophagus may occasionally be traceable to hiatus herniation with regurgitation, according to Chamberlin.[14]

Case 3. A 56-year-old housewife entered the hospital complaining of abdominal discomfort of about 30 months' duration. Originally these symptoms were very slight. An x-ray investigation at another hospital shortly after onset of the disturbance had demonstrated an oval 4-cm. tumor, with persistent deformity of the greater curvature of the stomach near the junction of its middle and distal thirds. The symptoms were so slight that operation was declined.

When first seen at the Cancer Section of the Westfield State Sanatorium, the patient had experienced persistence of symptoms. In addition, substernal pain frequently occurred, especially when she was in the recumbent position. Physical examination revealed a large irregular mass extending down to the umbilicus. Cachexia, ascites and edema of the lower extremities were observed. X-ray studies revealed fixation of almost all the greater curvature to a very large mass (Fig. 4). This mass was found to be separate from the liver and spleen. The adjacent gastric rugae were normal, that is, there was no fluoroscopic or film evidence that the tumor had involved the mucosa. The transverse colon and adjacent flexures were displaced downward and anteriorly (Fig. 5). Excretory pyelograms showed no urinary-tract abnormality.

Figure 4. *Case 3.*

A film showing deformity and elongation of the stomach from fixation to a mass — a retroperitoneal hemangioendothelioma — along the greater curvature.

Six months elapsed before the patient would consider hospitalization, although laparotomy was advised from the first.

Exploratory laparotomy revealed a large irregular cystic tumor about 18 by 22 by 10 cm. The main tumor mass arose in the region of the pancreas and projected into the lesser peritoneal sac. The mass was attached to structures about it, distally to 3 cm. below the level of the umbilicus and proximally to the liver and stomach.

Histologically the tissue was found to be typical of hemangioendothelioma, both by frozen and paraffin sections.

Figure 5. *Case 3.*

A film made during fluoroscopy to show the epiphrenic gastric pouch that resulted from hiatus herniation.

Comment. The occurrence of a large cystic tumor and ascitic fluid in this case simulated the abdominal enlargement of late pregnancy. The hiatus hernia may be assumed to have been related to the consequent increased intra-abdominal pressure. This assumption is verified by the lack of any such finding at the onset of symptoms, when an upper gastrointestinal examination was done prior to the time the tumor reached its final large size or ascites appeared. The frequency of abdominal enlargement from neoplastic disease, particularly ovarian tumors, affords this type of increased intra-abdominal pressure, which may assert itself by herniation of the stomach through the esophageal hiatus.

Conclusions

More careful clinical and roentgenologic attention to the diaphragm in patients with neoplastic disease is advocated.

Lack of pathognomonic physical signs of subphrenic abscess, neoplastic phrenic paralysis and hiatus herniation in these patients calls for thorough investigation of symptoms referable to the diaphragm and adjacent structures.

Fluoroscopy, films during and after fluoroscopy and fluoroscopic visualization of the barium-filled cardia are of established value and in fact are often essential for the diagnosis of these complications.

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CLINICAL NOTE

EMERGENCY TREATMENT OF TRAUMATIC EMPHYSEMA OF THE MEDIASTINUM

GERALD L. GAUDRAULT, M.D.,*

AND

DUNCAN M. CHALMERS, M.D.†

CONCORD, NEW HAMPSHIRE

A STUDY of the literature on traumatic emphysema of the mediastinum confirms the statement of Heuer[1] that "procedures directed to the mediastinum itself, with the idea of allowing the escape of air or to close the lesion from which the air is escaping, have not been numerous in the literature." He quotes Gatellier and Barbary[2] as reporting that 2 of their 3 patients died because lateral incisions under the clavicle did not permit satisfactory escape of the air. The third patient recovered following incision at the base of the neck, with separation of the pretracheal and peritracheal tissues. Heuer also states that Phocas and Apert[3] performed artificial pneumothorax in some cases, with eventual recoveries.

The effect of air in the mediastinum is not always serious. Fortunately, in the greatest number of cases the symptoms are mild, and Nature takes care of them with no help from the surgeon. In a few cases, however, the effects are very serious. Concerning these, Heuer[1] states: "The heart, great vessels and trachea may be compressed or dislocated, giving rise to urgent symptoms. These are marked agitation and anxiety, cyanosis, tachycardia, signs of suffocation, tumefaction of the base of the neck and a rapidly spreading emphysema." In such urgent cases the surgeon has to work fast to save the patient.

Babcock[4] states that emphysema of the mediastinum may seriously upset respiration and circulation, but that subcutaneous emphysema usually disappears spontaneously in a few days. Warbasse and Smyth[5] believe that emphysema occurring in connection with such wounds of the pleura usually requires no treatment; in most cases the air is absorbed, and if it should give distress, it may be liberated by incisions of the skin. DaCosta[6] makes a similar statement: "Emphysema usually disappears, but if it does not, make many small incisions and employ pressure." Eliason[7] admits that injury to the pleura and lung producing mediastinal emphysema may be the cause of death, but states that emphysema from this cause usually requires no treatment, disappearing in about ten days. Hertzler and Chesky[8] also found that emphysema in the tissues is soon absorbed. Watkins[9] and Stenbuck[10] follow the opinion of the preceding men and agree that if left alone the air will be absorbed naturally without the aid of a suprasternal-notch incision; if active measures are contemplated, both recommend artificial pneumothorax as the method of choice. On the other hand, suprasternal-notch incision with applications of a suction cup, according to Lenormant,[11] is necessary in most cases.

All cases of emphysema of the mediastinum do not fall into the hands of surgeons of wide experience, and are not treated in large metropolitan hospitals. What if a serious case falls into the hands of a surgeon who has never seen one like it? It surely is too late to start looking for literature on the subject, since cases are extremely rare and, hence, difficult to find. He can only go

*Member of active staff, New Hampshire Memorial Hospital, and of associate staff, Margaret Pillsbury General Hospital.

†Formerly resident, Pembroke Sanatorium, Concord, New Hampshire.

ahead immediately and do those things that, according to his senses, seem to be called for.

The following case is reported, not to present a masterpiece in chest surgery but to be of service, if possible, to someone who might be called on to save a patient's life under similar circumstances.

Case Report

A 63-year-old man fell off a scaffold and landed on his right thoracic region. One of us (D. M. C.) removed the patient to the hospital immediately.

Examination revealed a massive accumulation of subcutaneous air extending over the upper thorax, supraclavicular region, face and upper extremities. Perspiration was profuse. The temperature was 99°F., the pulse 100, the respirations 40, and the blood pressure 220/110. The chest was very tender over the right posterior thoracic region and right shoulder, and crepitus was present. The heart was slightly enlarged, but the sounds were of good quality. Abdominal examination was negative. It was thought that there were probably fractures of the right ribs, with puncture of the pleura and lung.

The examination was not prolonged, since the patient's condition was growing rapidly worse. Because the nearest chest surgeon was eighty miles away, it was decided to administer the best treatment possible under the circumstances.

Following a sterile preparation of the neck, a 5-cm. transverse incision was made, under local anesthesia, in the suprasternal notch. The subcutaneous tissues were separated by blunt dissection. Air bubbled through the wound after the subcutaneous fascia had been divided. By means of an inverted sterile glass funnel and rubber tube attached to an electric pump, suction was secured. Considerable relief was obtained at once, and the patient's color improved. Suction was stopped after several minutes, and the patient's condition grew worse again very rapidly. Suction was reapplied, and an artificial pneumothorax apparatus, located six miles away, was sent for. With this apparatus, about 1300 cc. of air was introduced into the right pleural space to collapse the lung. Suction was removed, and the patient's condition remained improved. Owing to the emphysema, no attempt was made to correct the condition of the ribs, and the patient was removed to his room at 8:00 a.m.

During the next 24 hours, suction was applied three times to relieve emphysema and discomfort. The respiratory rate dropped to 28, and the pulse to 96; the blood pressure rose to 145/100.

The following day the patient's condition had improved, and about half the subcutaneous emphysema had disappeared. Dyspnea was scarcely noticeable. The temperature was 100°F., the respirations 28, the pulse 88, and the blood pressure 150/88.

An x-ray film of the chest showed a complete collapse of the right lung, with displacement of the heart to the left, and three separate fractures, posteriorly, of the 3rd rib on the right side, with considerable displacement of a large posterior fragment. It also showed fractures of the 6th and 2nd ribs near the spine, with displacement.

From then on the patient showed steady improvement, the temperature, pulse and respirations dropping to normal on the 7th day. The right thoracic region was strapped with adhesive tape on that day. This might have been done before, but owing to the extensive emphysema, would have been relatively ineffective. The patient was discharged on the 9th day, free from pain and with the emphysema nearly gone. He was seen several months later, perfectly well and back at work; he did not complain of discomfort.

Summary

The successful emergency treatment of a patient with traumatic emphysema of the mediastinum is described.

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MEDICAL PROGRESS

CARDIOVASCULAR DISORDERS IN SCARLET FEVER*

CONRAD WESSELHOEFT, M.D.†

BOSTON

MEDICAL progress in scarlet fever has not been confined to the fields of bacteriology, immunology and chemotherapy. The cardiovascular disorders that arise in this disease have been the subject of numerous investigations, which are worthy of review.

MAJOR CLINICAL FINDINGS

The vascular disturbances of the eruptive stage of scarlet fever consist in dilatation of the peripheral capillaries of the skin — the exanthem — and those portions of the mucous membrane involved in the enanthem. Thus, the introduction to a discussion of cardiovascular disorders arising in the course of scarlet fever should begin with the paramount fact that the chief characteristic of the disease itself is brought about by the action of the toxin on the peripheral capillaries. With this in mind, one might expect that the heart as a highly specialized organ of this vascular system would be susceptible to attack by this toxin. As a matter of fact, the heart is under certain circumstances peculiarly susceptible to the toxic products of the scarlet-fever strains of streptococci, but this susceptibility in the vast majority of cases leads to no more harm than the rash itself.

TABLE 1. *Reported Incidence of Endocarditis and Pericarditis in the Course of Scarlet Fever, Compiled from Metropolitan Asylums Board Reports, London**

YEAR	CASES OF SCARLET FEVER	CASES OF ENDOCARDITIS	INCIDENCE OF ENDOCARDITIS %	CASES OF PERICARDITIS	INCIDENCE OF PERICARDITIS %
1907	22,096	129	0.58	17	0.08
1908	20,102	165	0.82	24	0.12
1909	16,191	118	0.73	11	0.07
1910	9523	88	0.92	12	0.13
1911	8438	63	0.75	14	0.17
1912	9793	31	0.32	3	0.03
1913	14,325	79	0.55	13	0.09
1914	21,006	87	0.41	17	0.08
Totals	121,474	760	0.63	111	0.09

*Now the County Council Hospitals; no published reports since 1914.

On the other hand, serious cardiovascular disorders may occur in the wake of scarlet fever; but the results of investigations indicate that these serious disorders are relatively infrequent as compared to those following rheumatic fever and chorea. Indeed, many — if not most — valvular defects found in the course of scarlet fever can be traced back with careful histories to a previous rheumatic or choreic infection.

The endocarditis that does originate from the hemolytic streptococcus of scarlet fever is a result of blood-stream infection and constitutes a bacterial endocarditis. Furthermore, in scarlet fever such blood-stream infection is apt to follow a local pyogenic process in the mastoid cells, associated with a lateral sinus thrombosis. But even with a blood-stream infection, such an endocarditis takes place very rarely. In fact, its infrequency in cases of bacteremia suggests that a previously damaged valve may be necessary. The commoner form of endocarditis seen in scarlet fever is of rheumatic origin.

TABLE 2. *Reported Incidence of Endocarditis in Scarlet Fever.*

	SERIES COMPLETED	CASES OF SCARLET FEVER	CASES OF ENDOCARDITIS	INCIDENCE OF ENDOCARDITIS %
Metropolitan Asylums Board, London	1914	121,474	760	0.63
Joe,[1] City Hospital, Edinburgh	1924	24,102	61*	0.25
McCollom, Place and Funk,[2] Boston City Hospital	1925	2000	13	0.65
Zischinsky,[3] Wilhelminen-Spital, Vienna	1930	20,000	11	0.05
Gordon,[4] Herman Kiefer Hospital, Detroit	1931	10,666	78	0.7
Imrie,[5] Belvidere Fever Hospital, Glasgow	1933	1616	6†	0.37
Wesselhoeft, Haynes Memorial Hospital, Boston	1939	12,820	58‡	0.45
Totals		192,678	987	(0.51)

*This figure includes pericarditis with endocarditis.

†All 6 had a rheumatic history and 2 had valvular lesions on admission.

‡Thirteen of these patients were known to have had valvular disease before scarlet fever; in 12 cases there is doubt whether the valvular disease preceded the scarlet fever.

*From the Harvard School of Public Health and the Haynes Memorial, Massachusetts Memorial Hospitals.

†Clinical professor of communicable diseases, Harvard University; associate professor of theory and practice, Boston University; physician, Haynes Memorial, Massachusetts Memorial Hospitals.

Clinical interest in endocarditis during scarlet

fever, therefore, resolves itself into a recital of its reported incidence. The accompanying tables give the incidence of both the bacterial and rheumatic types. Probably these include a certain number of unrecognized congenital defects. I am sure that this is true of my own earlier records. In Table 1, I have compiled the figures from 1907 to 1914 from the annual reports of the Metropolitan Asylums Board hospitals of London. Others have used the figures of isolated years, but this compilation shows the variation of incidence and its independence of the morbidity, as well as the relation of endocarditis to pericarditis. Table 2 is a compilation of published figures, including the extraordinarily low figure of Zischinsky[3] and the data regarding rheumatic history in Imrie's[5] series. My figures from the Haynes Memorial Hospital, like some of the others offered in Table 2, do not represent any consistent effort to ascertain a previous rheumatic history. Because of this review, subsequent cases are being carefully studied on this point, with the result that the findings more closely approximate those of Imrie. The total average in this substantial number of hospital cases is 0.51 per cent.

If one excludes those cases that have all the characteristics of rheumatic fever, the incidence of what may be termed a true scarlet-fever endocarditis with vegetations and permanent damage becomes exceedingly rare. Zischinsky[3] found only one such case among 20,000 cases of scarlet fever in the Wilhelminen-Spital in Vienna. He states that he agrees with his predecessors, Pospischill and Weiss, that scarlet fever plays no significant part in the etiology of valvular disease.

The relation of scarlet fever to rheumatic fever is a subject that has brought forth many theories. Both diseases are intimately related to the streptococcus, and rarely originate in tropical climates. In both, allergic hypotheses have been advanced to explain the symptoms.[6–8] The close clinical and immunologic relation of the hemolytic streptococcus to rheumatic fever has been brought out by Mote and Jones.[9]

In scarlet fever, there is uncontroverted evidence that the erythrogenic toxin is the product of certain strains of hemolytic streptococci, although there are those who continue to believe that a virus is in some way likewise responsible. In rheumatic fever, a nonhemolytic streptococcus is incriminated in much the same way as streptococci in scarlet fever before the discovery of the Dicks. Only recently evidence has been presented in support of the hypothesis that a virus is associated with the streptococcus in rheumatic fever.[10, 11] It is generally conceded that the streptococcus, often in the form of a tonsillar infection, predisposes the tissues to a latent rheumatic-fever infection. If this hypothesis is correct, an infection with scarlet fever might likewise activate any latent rheumatic-fever element, and there is ample clinical evidence that it does so.[5, 12, 13]

If an endocarditis develops from two to twelve months after a tonsillitis, it is promptly diagnosed as rheumatic heart disease, but if endocarditis develops in the same length of time after scarlet fever it is oftener diagnosed as a missed scarlet-fever heart lesion. Such a diagnosis is not in keeping with present-day knowledge of scarlet fever and rheumatic fever. An established valvular defect coming into existence late after scarlet fever should be considered of rheumatic origin.

In connection with the rheumatic origin of endocarditis in the course of scarlet fever, it should be kept in mind that scarlet fever is a disease largely of early childhood, and therefore many potential rheumatic patients come down with scarlet fever before their first attack of rheumatic fever. Furthermore, older patients are less likely to develop valvular disease than children in the course of rheumatic-fever attacks.[14] Consequently, these two factors reduce the chances of developing rheumatic endocarditis in the course of scarlet fever. Of course, if the valves are already damaged by a previous attack of rheumatic fever, the endocarditis cannot be said to have originated with the scarlet fever, but is merely brought into renewed activity by it.

Since Salinger and Leonard's[7] excellent review up to 1930, the rheumatic origin of nonseptic endocarditis in scarlet fever has become quite generally accepted. According to White,[14] the incidence of heart disease in rheumatic fever is 85 per cent, and in chorea 49 per cent. Granting that this estimate may be too high, the differences between the incidences in these two diseases and that reported in scarlet fever is only too obvious.

Moltschanow[15] reports 17 cases of rheumatic endocarditis in the course of scarlet fever in Moscow. In 2 the endocarditis flared up in the second week; in the other 15, between the third and eighth weeks. In 14 it was simultaneous with the joint symptoms. In only 3 had there been a previous attack of rheumatic fever, yet in 7 out of 13 in which an accurate family history was available there was a definite family history of rheumatic fever. Imrie's[5] studies are even more impressive. In 1696 cases of scarlet fever in Glasgow he had 6 patients with endocarditis, all of whom gave a rheumatic history, and in 2 a valvular lesion was found on admission to the scarlet-fever ward.

A true severe myocarditis such as occurs in diphtheria is rare in the course of scarlet fever. In the majority of cases, severe myocarditis is due to a mixed infection with the diphtheria bacillus, a not uncommon complication. Diphtheria confined to the anterior nares, the so-called "larval type," has a characteristic lack of toxicity. But diphtheria infections of the postnasal space give rise to the highest percentage of myocarditis.[16] These are often missed. There have been 9 cases of severe myocarditis at the Haynes Memorial Hospital among 12,820 cases of scarlet fever. Six of these had positive diphtheria cultures, and of 3 septic cases 2 showed heart block. Rosenbaum[17] reports 4 cases of myocarditis with diphtheria as a mixed infection, and 2 fatal cases with septic complications. One sudden death on the fourteenth day is reported, with myocarditis found at autopsy.[18] Of course, a severe myocarditis could be brought about by any severe mixed infection, but in my experience a culture from the postnasal space in these cases is very apt to show virulent diphtheria bacilli. An investigation of this point should always be carried out when severe myocarditis develops in the course of scarlet fever.

Pericarditis may occur as the result of bacteremia, in which case streptococci are found in the pericardial fluid. Here the pathology is no different from that found with any other similar infection with hemolytic streptococci and needs no special description. The same general statement applies to the rheumatic form of pericarditis, the discussion of which belongs to rheumatic fever rather than to scarlet fever. The incidence of pericarditis in the course of scarlet fever may be seen in Table 1.

Minor Clinical Findings

The benign effects of scarlet fever on the heart, which are alluded to above as of no more consequence than the rash itself, have long been of interest to students of scarlet fever, and this interest has been reawakened by the use of the electrocardiograph.

The benign cardiac signs occurring in the course of scarlet fever constitute a transient affair lasting from a few days to about three weeks, which in itself does not disturb the patient. It has been described under such terms as "benign myocarditis," "functional myocardial insufficiency" and "benign endocarditis," but it is best known as the "scarlet-fever heart."

The clinical picture of the so-called "scarlet-fever heart" is well known. It consists principally of the development of murmurs usually without irregularity in rhythm. This appears either during the eruptive stage, or more commonly between the ninth and twenty-fourth days of convalescence, that period described by Schick[19] as the "second danger period." The first sign is usually a split first sound. Abnormalities are likely to be noticed when the patient is first allowed out of bed, because the attention of the physician is focused on the heart at this time, and the increased activity tends to augment the signs. The murmur is so variable in time and character that any attempt to describe it is futile. Indeed, each author who has attempted to do so has given a different version. It can occur in systole or diastole, but is commoner in systole. Some have emphasized that its occasional harshness is somewhat suggestive of a slight friction rub at the base, an observation corroborated on the wards of the Haynes Memorial Hospital. In very rare cases the existence of a mitral stenosis would be suggested were it not for its sudden appearance. Of course, a true mitral stenosis takes months to develop. If joint pains accompany the appearance of the murmur, there may be a sharp rise in temperature, with tachycardia. The heart rate is not necessarily increased with the advent of these abnormal sounds. However, quite independently of these sounds there may occur a persistent tachycardia or even a relative bradycardia. Occasionally there is an abrupt drop in heart rate from 120 to 60 without any symptoms whatever. There is rarely any cardiac enlargement, and there is no precordial pain or discomfort. Irritability of the pacemaker is often pronounced. All these clinical signs may entirely disappear by the end of a week, and in the more marked cases in three or four weeks. The more pronounced physical signs are sometimes accompanied by one or more alterations in the electrocardiogram, but since this does not always follow, they are not dependent on each other, although I assume that they arise from the same source.

Benign cardiac murmurs were reported in 70 per cent of scarlet-fever cases by Lederer and Stolte,[20] in 22 per cent by Hirsch,[21] in 5 per cent by Rosenbaum[17] and in 4.7 per cent by Gordon.[4] In the last three years at the Haynes Memorial Hospital we have found transient murmurs in 9 per cent. In the preceding five years, they occurred in 6 per cent. The wide variations in the results of these observations obviously depend on the interpretation of the heart sounds by the attending physicians, as well as on epidemiologic factors.

It has long been recognized that the complications of scarlet fever vary greatly in different epidemics. This variation appears to be exceptionally marked in benign heart disorders.[2] In fact, in one epidemic, Pospischill[22] found cardiac abnormalities with surprising frequency at the outbreak,

and then suddenly this complication ceased to appear. This supports accumulating evidence that the incidence of various complications in this disease is related to the type of streptococci[23] or to their symbiosis with other infections.[24]

Again and again the pronounced character of these murmurs suggests the possibility of endocarditis, but their benign course eliminates this diagnosis. In the absence of septicemia and unless the patient has a previous history or a family history of rheumatic fever and unless a high sedimentation rate in conjunction with polyarthritis and fever is present, I have come to take the stand that even the most marked murmurs arising in the convalescence of scarlet fever are benign in character. Under these circumstances, the chances of being wrong are exceedingly remote.

Electrocardiographic abnormalities appear to vary in their frequency quite as much as abnormal auscultatory findings. Thus Faulkner, Place and Ohler[12] found abnormal electrocardiograms in only 11 of 171 cases of scarlet fever at the Boston City Hospital. Berger and Olloz[25] in Switzerland found alterations in 14 out of 66 simple scarlet-fever cases. On the other hand, Wickström[26] reported 86 abnormalities in 100 cases of scarlet fever at the Epidemic Hospital in Stockholm, in which those showing only a negative T wave in Lead 3 were excluded. The frequency with which abnormal electrocardiograms are reported by this author leaves one skeptical of his interpretations. The electrical alterations that Wickström offers as evidence of myocarditis are by no means convincing, and consequently the records would have to be checked carefully before one could accept his interpretations of what actually constitutes deviations from the normal.* The various disturbances enumerated by him showed much the same relation to the toxic stage as they did to the occurrence of late complications, no one complication showing any more of these electrical changes than another. These changes were seen with equal frequency among those toxic cases receiving antitoxin or convalescent serum and in those in which this treatment was not given. Furthermore, the alterations observed in the convalescent stage showed no consistent association with changes in the pulse and temperature. In 19 cases auscultatory signs accompanied the electrocardiographic alterations, but at other times they were entirely independent of one another. No typical alterations were apparent, but Wickström believed that the changes were concerned particularly with the conduction system in the left ventricle. In 40 per cent, these alterations disappeared during convalescence, in 38 per cent during the next six months, and in 28 per cent they were still present after seven and a half months. However, with the interpretations questioned, these observations lack the necessary background to carry weight.

Shookhoff and Taran[27] in a study of 78 normal children found slight slurring and widening of the QRS complex in Lead 1 or Lead 2 in 35 per cent, inverted T wave in Lead 3 in 25 per cent and abnormally deviated axis in 3 per cent. From ten to fourteen years of age, there was a definite decrease in the incidence of an inverted T wave in Lead 3. In 50 mild scarlet-fever cases these authors found normal P waves and a normal QRS in Lead 1 and Lead 2 and alterations in the T wave in Leads 1 and 2 in 10 per cent and an inverted T wave in Lead 3 in 40 per cent. They did not consider these changes to be evidence of myocarditis.

Van Buchem and Daniels[28] found a normal T wave in Lead 3 in 133, or 63 per cent, of their 211 cases of scarlet fever. It was diphasic in 13. These T-wave alterations were rarely present on admission, and in 105 they had disappeared before the end of the isolation period. These electrocardiographic findings are not peculiar to scarlet fever, nor do they constitute proof of myocarditis.

This benign character of the scarlet-fever heart is striking in comparison with the cardiac damage in rheumatic fever even when one knows that physical signs in the latter may disappear.[29, 30] Indeed, the physical signs of the scarlet-fever heart are of a will-o'-the-wisp character as compared with those of rheumatic fever.

The etiology of these benign cardiac signs in scarlet fever has been the subject of much discussion. They have been ascribed to loss of tone of the heart muscle and to dilatation. To these may be added the factor of increased blood flow. Indeed, I am inclined to believe that in some cases the abnormal sound may represent only a forceful heartbeat. On the other hand, some of the coarse murmurs at the base suggest that the signs originate in the epicardium. Probably in some cases the abnormal sounds are simply due to an overactive heart, in addition to a little transient toxic dilatation. The term, "myasthenia cordis," has been used. It has been asserted that the scarlet-fever heart is always associated with loss of body weight,[20] and by others that it is the result of "impoverished" blood. These last two relations have been carefully studied by von Kiss and Malaguzzi-Valeri[31] and thrown into the discard for lack of support.

First of all, Are these electrocardiographic changes peculiar to scarlet fever? They most cer-

*Wickström's series of 100 cases of scarlet fever was reported as showing atrioventricular disturbances in 67; intraventricular disturbances in 59, of which 25 showed lengthened QRS time and 46 deviated axis; inverted T waves in 33; and at least one of these abnormalities in 86.

tainly are not, since they are found also in many acute infections, such as tonsillitis, rheumatic fever, diphtheria, typhoid fever and pneumonia. Nor can they be said to occur with greater frequency in scarlet fever than in these other infections. They are, however, definitely related to the eruptive stage, and appear again in convalescence with or without the fever of complications, and unrelated to any particular complication. The source of these minor abnormal electrical disturbances, variable heart sounds and sudden changes in rhythm appears to be a local effect of the toxin or of some by-product of streptococcic invasion circulating in the blood stream.

Allergy has been advanced as an explanation for everything in scarlet fever, from the rash to all complications. But it is said that the purified toxin is not allergenic.[32] Quite aside from the toxin, there are many other toxic products evolved by the growth of hemolytic streptococci in vivo. Furthermore, the initial damage to the reticuloendothelial cells in the eruptive stage or an antigen-antibody reaction may possibly be a factor in the causation of these benign cardiac signs. Fahr[33] is of the opinion that any attempt to work up an allergic hypothesis for the scarlet-fever heart is taking liberties with the present conception of hypersensitive tissues. However, a violent local antigen-antibody reaction affords the best explanation of the etiology of purpura hemorrhagica[34, 35] and acute glomerulonephritis,[36] both of which are essentially late vascular complications of scarlet fever. Zischinsky[37, 38] has reported 4 cases of edema of the skin due to blood-vessel damage late in the course of scarlet fever without any evidence of nephritis. This might be ascribed to endothelial-cell damage.

Pathology

Practically all autopsy material is from septic cases and therefore, of course, represents a toxic condition of the heart common to all fatal streptococcal conditions in which pus formation prevails. Scarlet-fever patients rarely die of the toxin, except in parts of Roumania. The heart in these early fatal cases may escape injury if death occurs in forty-eight hours, just as it may in early deaths from diphtheria. Here death is due to the effect of the toxin on the cerebrum, with delirium and coma accompanied by a very marked tachycardia. If death occurs later in these severe toxic cases, small hemorrhages may be found in the heart, as well as injection of the blood vessels about the bundle of His.

Fahr[33] found perivascular granulomas with large cells "not exactly identical with the giant cells found in rheumatic fever but very similar to them." Stoeber,[39] on the other hand, found that the blood vessels of the myocardium were primarily injured along with the perivascular connective tissue, but to a much less extent than in diphtheria, because severe degeneration of the muscle fibers is never brought about. To him, there is no confusion between the pathology of scarlet fever and that found in diphtheria or rheumatic fever. Magladery and Billings[40] state that in scarlet fever one finds a diffuse interstitial myocarditis, whereas in diphtheria the lesion is primarily parenchymatous with secondary interstitial involvement, and that in rheumatic fever the myocarditis is almost entirely perivascular in the form of nodes. Aschoff nodes will be well developed if the patient has had a previous attack of rheumatic fever, but if the first attack occurs during the course of scarlet fever, these rheumatic elements will be immature.

Since the typical scarlet-fever heart of the second and third weeks is a characteristically benign condition, the patient who comes to autopsy must succumb from some other complication, which, in its development, would mask any underlying slight lesion if one existed. Therefore, one is not justified in offering explanations based on post-mortem findings in toxic, septic or rheumatic cases.

Treatment

Endocarditis and pericarditis of rheumatic origin require the usual treatment outlined under rheumatic fever, with salicylates and digitalis when indicated. However, patients with a rheumatic history who develop pain and swelling in the joints while suffering from scarlet fever often run an unfavorable course and may not respond well to salicylates.[5] Doses in the maximum scale are frequently necessary to control pain. Digitalization, on the other hand, may be relied on when indicated in cases with old valvular lesions showing congestive failure or auricular fibrillation.

In *endocarditis* and *pericarditis of bacterial origin*, sulfanilamide should be given. I am speaking here on the basis of a very favorable experience with bacteremia in scarlet fever treated in this way.[41] The higher scale of blood level should be used.[42] Needless to say, if the bacteremia has proceeded to a vegetative endocarditis, the outlook is exceedingly unfavorable. In very rare cases, recovery has occurred, and immunotransfusion along with sulfanilamide offers a hope that could never be entertained before. Tapping the pericardium may be resorted to, but should be attempted only by experienced hands.

A certain amount of toxic myocarditis accompanies these cases. I have never known drugs of the digitalis group or Coramine, caffein or camphor in oil — or I might say any drug other than sulfanilamide — to exert any appreciable beneficial effect whatever in these septic cases. Furthermore,

I am under the impression that digitalis has often made a serious condition of this kind worse rather than better.

Patients with myocarditis resulting in cardiac dilatation and failure should receive digitalis, as recommended by Hecht,[43] but I have not yet seen such a condition in the course of 12,000 cases of scarlet fever, except through a profound secondary streptococcal septicemia or a mixed infection with diphtheria bacilli. A case of complete auriculoventricular dissociation following scarlet fever is described by Bernstein[44] in which "cardiac decompensation [persisted] despite the use of all known therapeutic measures." Although I have not seen such a case, it is to be noted that Bernstein's patient was discharged from one of the best contagious hospitals, after the subsidence of the scarlet fever, with what appeared to be a normal heart. The electrocardiograph was not used in this case during the course of the disease.

Benign carditis, the so-called "scarlet-fever heart," needs no further treatment than rest. This applies to the cases that show a well-marked split first sound, obvious murmurs or persistent tachycardia. Abnormal electrocardiographic findings of a mild nature can be safely ignored, and the customary treatment of scarlet fever carried out. The more marked cases require rest in bed until the signs disappear. If the signs appear again when the patient is allowed out of bed, the rest should be resumed for another week, and if they again appear the patient is allowed increased activity of the most gradual form and under close observation. No medicine is necessary. It is assumed that all steps have been taken to rule out the existence of rheumatic fever.

The author expresses his indebtedness to Dr. Paul D. White for the clarification of many of the uncertainties in the field of cardiology that beset one who deals with the problems of acute infections.

315 Marlboro Street

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27221

PRESENTATION OF CASE

A fifty-three-year-old Polish housewife entered the hospital complaining of abdominal pain.

The patient felt perfectly well until the onset of general malaise six months before admission. There was, however, no specific complaint until two months before admission, when an aching pain developed in the upper abdomen, which radiated to the back and seemed to be initiated by food and relieved by fasting. Anorexia and weight loss soon appeared, so that at the time of admission her weight had dropped 40 pounds. Finally, a physician was called, who felt a mass in the patient's abdomen and sent her into the hospital.

At no time had the patient noticed chills, fever, nausea, vomiting, jaundice or change in the character of her stools. Although there were no subjective urinary symptoms, the urine had been dark for the previous two months.

The past and family histories were irrelevant.

On examination the patient was well developed and pale, and showed evidence of recent weight loss. The heart and lungs were essentially normal; the blood pressure was 175 systolic, 90 diastolic. A large, tender, freely movable, superficial mass was palpable in the right upper quadrant of the abdomen, which moved with respiration. Tenderness was present in the right costovertebral angle. A pelvic examination was negative.

The temperature was 99°F., the pulse 85, and the respirations 20.

The urine showed a + test for albumin and an orange sugar reaction. The sediment contained from 4 to 6 white cells per high-power field. The blood showed a red-cell count of 3,200,000 with a hemoglobin of 70 per cent, and a white-cell count of 7500. The nonprotein nitrogen of the blood serum was 28 mg., the sugar 272 mg., and the protein 6.9 gm. per 100 cc.; the chlorides were 96.3 milliequiv. and the carbon dioxide combining power 26.2 milliequiv. per liter. The serum van den Bergh was normal.

X-ray films of the chest and a barium enema were negative. With a Graham test there was no filling of the gall bladder, and the right kidney appeared enlarged; no stones were seen.

An intravenous pyelogram revealed the right kidney to be about twice the size of the left and slightly lobulated. The dye was excreted promptly on both sides and filled apparently normal pelves and ureters. The substance of the right kidney appeared unusually large for the size of the pelvis; the calyxes were a little long. A retrograde pyelogram on the right side was unsatisfactory because of motion. The spiderlike formation of the upper and middle calyxes was again visible.

An electrocardiogram showed normal rhythm at 100, with a PR interval of 0.15 second. There was low voltage in Lead 3 and a slightly inverted T_3; Lead 4 was normal.

A cystoscopic examination one week after admission revealed nothing abnormal. Four days later an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ROBERT R. LINTON: My function in discussing this case, of course, is to tell you what the mass in the right upper quadrant was. There are four definite possibilities that must be considered with a right upper-quadrant tumor. One of these is an enlarged gall bladder or an associated increase in the size of the liver, which we shall consider as one condition. Another is a kidney tumor. A third is a tumor of the hepatic flexure of the colon, or perhaps the ascending colon, or the beginning of the transverse colon. And a fourth is a tumor in the region of the pylorus.

To begin with the last possibility first, we have no evidence that the patient had any special gastrointestinal symptoms except for anorexia and weight loss. She felt worse after eating food, and was relieved by not eating; perhaps this indicates some interference with her digestive processes. I am a little at a loss to know why they did not do a gastrointestinal series. Apparently they did not, so that we can get no help from the x-ray findings in regard to the stomach and pyloric region. I doubt very much whether this condition was associated with the stomach, however, and I should like to pass on to the tumors of the colon. The hepatic flexure is one of the hardest parts of the colon to visualize by x-ray. We have the statement, however, that a barium enema was negative, a finding which accords with the fact that the stools were normal. Furthermore, I should not expect tumor of the hepatic flexure to be as freely movable as this was. It is possible to have a carcinoma of the cecum in which the right colon is very freely movable, that is, not fixed to the abdominal wall as it normally is. It would therefore be possible to move such a carcinoma of the cecum around quite freely. In view of the nega-

tive barium enema and the normal stools, I do not believe that this was a tumor of the colon.

The third possibility to consider is a kidney tumor, and there was evidence by x-ray and intravenous pyelogram that there was an enlarged kidney on the right. It seems unlikely from the description, however, that this could possibly have been a kidney tumor, since it was described as a superficial mass and was very freely movable. The urine examination does not help us very much. The patient did have diabetes, judging from the urinary findings and the blood-sugar value, but I do not believe that had anything to do with the diagnosis of tumor in the right upper quadrant.

The fourth possibility, of course, is the gall bladder. Was this mass an enlarged gall bladder? In favor of that is the location and size of the tumor, and the fact that it was described as being fairly superficial and freely movable. I am a little surprised that the patient had lost 40 pounds in weight, if this was simply an enlarged gall bladder. We have additional x-ray evidence that the gall bladder was not visualized, that is, the Graham test was positive. Because of these findings, I am going to make a diagnosis of hydrops of the gall bladder.

Dr. George W. Holmes: So far as the x-rays are concerned, the interest is centered around the gall bladder and kidney. I shall not take the time to show the chest and enema films, which were reported as negative. The Graham test, like any test in which one must make a positive diagnosis on negative findings, must always be taken with a grain of salt. If this patient had taken food during the interval, or if anything had gone wrong with the test, we should report it as a positive finding. The most striking thing is the enormous size of the right kidney. One occasionally sees a large kidney as an anatomic variation, but there is also almost invariably a small kidney on the other side. This patient's left kidney is approximately normal in size and shape, and the right kidney is not only more than twice that size but also rather round. The injected pelvis does seem to be displaced upward a little, and the upper calyx is elongated but is within normal limits. An anatomic variation might account for that, but I do not believe it would account for the size and shape of that kidney, so that I should be very much surprised if there was not disease in the right kidney. Whether that was the clinical diagnosis is another question. It does not seem likely.

Dr. William B. Breed: I take it when you say hydrops that you mean a gall bladder distended with fluid.

Dr. Linton: Probably clear fluid.

Dr. Breed: Then should you not want to give some explanation of the obstruction, such as a stone, cancer of the ampulla or something of that sort?

Dr. Linton: I do not believe that hydrops of the gall bladder ever occurs without a stone impacted in the cystic duct. With a common-duct stone there is always bile in the gall bladder, sometimes so-called "white bile," but there is seldom if ever a huge dilated gall bladder. Hydrops to the surgeon means obstruction of the cystic duct, practically always due to a stone and nothing but clear mucus within the gall bladder.

Dr. F. Dennette Adams: How often do you see that without superimposed acute infection?

Dr. Linton: I should say quite often. There is seldom infection in this type of gall-bladder disease.

Dr. Reed Harwood: Do you think it would account for malaise, weight loss and anemia?

Dr. Linton: The weight loss bothered me. It seemed unusual.

Dr. Breed: The diabetes might cause loss in weight, might it not?

Dr. Linton: Yes, it might. The question is, How long was the diabetes present?

Dr. Richard H. Sweet: The X-ray Department and some of the house staff were much impressed by the size of the kidney, but those who paid attention to their sense of touch would certainly have made a diagnosis of hydrops of the gall bladder. I do not believe one could have called it anything else. We operated with that diagnosis and that is what the patient had, but on freeing up the gall bladder I discovered that there was a mass of abnormal tissue in the region of the cystic duct and ampulla. It appeared to me like carcinoma. An impacted stone in the cystic duct obstructed the gall bladder. Under the circumstances it seemed to me better surgery to take it out than to drain it. We did a simple and easy cholecystectomy. The kidney on palpation was definitely large, but I could not ascertain whether there was tumor in it.

Clinical Diagnoses

Carcinoma of gall bladder.
Diabetes mellitus.

Dr. Linton's Diagnoses

Hydrops of the gall bladder, with stone impacted in the cystic duct.
Diabetes mellitus.

Anatomical Diagnoses

Carcinoma of the gall bladder.
Hydrops of the gall bladder.
Stone in the cystic duct.

Pathological Discussion

Dr. Tracy B. Mallory: The gall bladder had a very thick wall, and sections of it showed adenocarcinoma of a very anaplastic character. The network of lymphatics between the gall bladder and the liver is very rich. Extension of the liver occurs so easily in cases of carcinoma of the gall bladder that chances of surgical cure are minimal. Grossly there was no obvious invasion of the liver.

Dr. Sweet: There was none, but I was certain that cancer must have been left behind, in shelling it out from the adjacent tissues. The common duct was not involved.

Dr. Benjamin Castleman: Had the hydrops been formed by the stone impacted in the cystic ducts?

Dr. Sweet: Yes.

Dr. Holmes: You still do not know about the kidney?

Dr. Mallory: No.

Dr. Holmes: I am not convinced that it was not abnormal.

CASE 27222

Presentation of Case

A sixty-seven-year-old man entered the hospital complaining of extreme weakness.

The patient was brought to the hospital in an ambulance, and at the time of examination displayed extreme air hunger and was unable to speak above a whisper. It appeared that three weeks before admission he had suffered a "fainting spell," and since that time had remained in bed because of an ever-increasing weakness. During these weeks before entry, he had several chills and suffered from frequency of urination, small amounts being passed at a time, with sudden stopping and starting of the stream. He had not noticed a change in the color of the urine. For the previous year he had been aware of exertional dyspnea, and had reputedly been helped by digitalis a few months before entry.

On examination the patient was well developed and lean, with a dry pale skin, dirty tongue and uremic breath. The heart was not enlarged to percussion, and the sounds were distant and of poor quality; the blood pressure was 120 systolic, 80 diastolic. The lungs were normal. Abdominal and rectal examinations were negative. The bladder could not be palpated or percussed. The prostate was not enlarged. There was no peripheral edema.

The temperature was 100°F., the pulse 80, and the respirations 40.

The urine was acid, the highest specific gravity being 1.015; it showed a ++ test for albumin, and the sediment contained a few red cells and many white cells per high-power field. A culture yielded a moderate growth of colon bacilli. The blood showed a red-cell count of 2,850,000 with 55 per cent hemoglobin, and a white-cell count of 28,700 with 91 per cent polymorphonuclears. The nonprotein nitrogen of the blood serum was 90 mg., and the protein 67 gm. per 100 cc. The chlorides were 117.6 milliequiv. and the carbon dioxide combining power 12.9 milliequiv. per liter, and the calcium 7.7 mg. and the phosphorus 4.2 mg. per 100 cc.

X-ray films of the chest and abdomen were negative.

An electrocardiogram showed sinus tachycardia (110–120), a PR interval of 0.18 second and a tendency to low voltage. ST_1 and ST_2 were sagging, and a few of the ventricular complexes had a slightly different form from usual. In Lead 3, some complexes were upright, and others inverted, but these changes were believed to be due to respiration. The T waves were low or inverted.

The patient was given intravenous fluids, digitalis and sodium citrate; closed drainage of the bladder and irrigation with potassium permanganate were instituted. On the following day, the temperature dropped to normal, but the respirations were still sighing and rapid. The urine remained about the same, although the number of white blood cells was much less. With a fluid intake of 4500 cc., the urinary output was 1500 cc., and this ratio was maintained throughout hospitalization. On the third hospital day, the temperature rose to 104°F. and the pulse to 150. Rales were present at both lung bases, and the calves were found to be tender on pressure and during forced dorsiflexion of the feet. An x-ray film of the chest showed increased density on the left side behind the heart, suggestive of consolidation. The next day the left leg was red, swollen and tender; the nonprotein nitrogen had risen to 130 mg. per 100 cc.; the chlorides were 114.3 milliequiv. and the carbon dioxide combining power 17.3 milliequiv. per liter. Peripheral edema gradually increased and involved the hands; an infected bulla developed on the left foot; terminally the nonprotein nitrogen was 143 mg. per 100 cc. Death occurred on the ninth hospital day.

Differential Diagnosis

Dr. Richard J. Clark: We are given very little information about the past history of this patient, and no inkling as to whether he had any previous renal difficulty. We first come to the story of dyspnea, which was supposedly helped by digitalis during the previous year. Yet when the patient was examined in the hospital the heart did not appear to be enlarged. The sounds were rather weak and of poor quality, as we might expect in a man of his general debility, but there were no pathognomonic signs on entry to suggest any specific primary heart difficulty. We are aware of no history of coronary or anginal pain. The electrocardiogram might suggest some degree of myocardial disease or of coronary insufficiency, but nothing specific. This makes us rather suspect that the weakness and dyspnea during the year prior to entry might have been associated with developing anemia and the beginning of nitrogenous retention, rather than being dependent on a primary cardiac difficulty. The fainting spell three weeks before entry is not sufficiently reported to give any specific clue of its nature. It may have represented a small coronary thrombosis, but there is nothing in the electrocardiogram at the time of entry that would bear that out. It seems very possible that this may have marked the beginning of an infection.

The patient entered the hospital in a markedly uremic and acidotic state, as evidenced by the physical examination and by the laboratory findings. He was very much dehydrated, and in spite of his dehydration the specific gravity of his urine apparently did not go above 1.015. He had a fairly marked degree of what I suppose was secondary anemia. There is no description of the blood to suggest any specific type of anemia. I suspect that this degree of secondary anemia probably went back farther than the three weeks of the acute illness described here, and that it was associated with a more chronic situation, which had been brewing for some time prior to entry.

With all these findings, my first thought is that the patient very probably had a chronic glomerulonephritis that had been going on for some time and was passing into the final stages of renal failure at the time he came to the hospital. He had a low blood pressure, but I suspect that before his state of marked weakness on entry it may well have been higher than the record indicates. It would be of interest to know what the eyegrounds showed, and whether there was evidence of old chronic vascular disturbance.

During the three weeks prior to entry, there was definite evidence of urinary-tract infection, with frequency and chills. We are told that the patient had some trouble in starting and stopping his stream. This is not a very striking symptom in view of his debility. We are told that his prostate felt normal by rectum. Of course, we cannot tell what the median lobe may have been like. There was no cystoscopic examination or x-ray examination to give any lead as to the nature of the possible block in the urinary tract. The patient might have had an old stricture that flared up with the infection. At any rate, we know he had a definite colon-bacillus infection, which I am inclined to believe was primarily in his bladder. He may have had some degree of ascending urinary-tract infection, and yet he did not have any high fever at the time of entry. There is no record of pus, casts or cell clumps in his urine, findings that we might have expected with a severe degree of pyelitis or with pyelonephritis, which also has to be considered. I do not see how we can make any such positive diagnosis. Also no mention is made of renal pain. Furthermore, on the day after entry to the hospital when the patient was put on drainage and the bladder irrigated, the white cells in the urine decreased and the temperature also dropped. In spite of this, he still had marked signs of acidosis and uremia. For these reasons I am inclined to interpret this as a secondary infection in the urinary tract, which was probably not the primary cause of his difficulty. I believe that he probably had a cystitis and possibly some degree of ascending infection superimposed on previously damaged kidneys.

The question arises whether he had any other type of renal lesion. Certainly, with a story of intermittent blocking of the urinary flow, we must think of anything that produces hydronephrosis, possibly a secondarily infected hydronephrosis, which might have accounted for a fairly complete renal failure toward the end. We might also think of polycystic kidney or cancer in the course of the urinary tract. There is no history of any gross hematuria, a fact that is somewhat against these diagnoses, and no story on physical examination of any enlarged or tender kidneys, and I gather from the abdominal plates that no enlarged kidneys were made out. If the patient had been in better health, we certainly should like to have seen a pyelogram, but with the evidence at hand I do not believe that there is any definite basis on which we can make a diagnosis of any other type of kidney disturbance. The urinary output failed to keep pace with the intake, and he developed edema, evidence of water as well as nitrogenous retention, as we might well find in the terminal stages of glomerulonephritis with involvement of

the tubules as well. Under treatment there was practically no improvement of the uremia and very little change in the acidosis.

On the third hospital day, there was a sudden rise in pulse and temperature, with rales beginning at the lung bases. X-ray films at this time are said to have revealed an area of consolidation in the left chest behind the heart. Coincident with this, signs and symptoms indicative of phlebitis developed in both legs, most prominently on the left.

This brings us to the question of whether, with the sudden rise in pulse and temperature, the patient developed a pneumonic process in the lungs, or whether this represented pulmonary infarction. With the obvious evidence of phlebitis, it seems to me that infarction is considerably more likely than pneumonia. It also seems unlikely that a man so obviously moribund would have lived as long as six days after the onset of a terminal pneumonia. To be sure, there was no pain, hemoptysis or increased dyspnea; but these factors are not necessary to make the diagnosis of pulmonary embolism, which I believe the patient had.

The infected area on the left foot strongly suggested the presence of terminal septicemia, which may well have occurred with a uremic death of this type. I should say that the diagnoses were chronic glomerulonephritis, with uremia and acidosis, a fairly severe secondary anemia, cystitis, possibly ascending pyelitis, possibly median-lobe prostatic obstruction, phlebitis of the left leg, recent terminal pulmonary embolism, terminal septicemia and possibly coronary sclerosis.

Dr. Tracy B. Mallory: In any case of renal insufficiency there is always room for a wide range of clinical diagnoses. Does anyone wish to suggest any other form of renal disease as a possibility?

Dr. Helen Pittman: Was any search made for Bence-Jones protein?

Dr. Mallory: I do not believe so. It was not recorded.

Dr. Benjamin Castleman: I should like to ask whether Dr. Clark thinks this man's age might be good evidence against chronic glomerulonephritis.

Dr. Clark: Yes; of course that would be a factor against it, but does not necessarily rule it out. Nephrosclerosis would be more likely at this age.

Dr. Bernard Jacobson: I should like to ask whether Dr. Clark is not worried by the water retention. Do you think that is common in terminal uremia?

Dr. Clark: It may be present in a terminal complete renal failure involving both the glomeruli and tubules.

Clinical Diagnoses

Chronic nephritis.
Uremia.
Thrombophlebitis of legs.

Dr. Clark's Diagnoses

Chronic glomerular nephritis, with uremia and acidosis.
Secondary anemia.
Cystitis, possibly with ascending pyelitis.
Prostatic obstruction?
Phlebitis of leg.
Pulmonary infarction.
Terminal septicemia.
Coronary sclerosis?

Anatomical Diagnoses

Acute and chronic pyelonephritis.
Bacterial endocarditis (colon bacillus).
Rheumatic endocarditis, healed mitral.
Pulmonary edema.
Thrombophlebitis, bilateral popliteal, left femoral and iliac.
Cholelithiasis.
Cellulitis, left foot.

Pathological Discussion

Dr. Mallory: The diagnosis on the wards was the same as Dr. Clark's. At post-mortem examination the outstanding findings were in the kidneys, which were extremely enlarged, the pair of them weighing 540 gm. The capsule stripped quite readily, and it immediately became apparent that both kidneys were filled with abscesses of all sizes and ages. The pelves were not significantly dilated. The bladder showed a mild cystitis. The prostate was normal. There was therefore no particular evidence that this infection of the kidneys was ascending in character. The heart showed slight old deformity of the mitral valve and also a few fresh vegetations, bacterial in character. The post-mortem culture showed colon bacillus, a finding that we often tend to discard, but it did occur in a pure culture, and cultures from the renal abscesses also showed colon bacillus in pure culture, so that I am inclined to think this was significant and that the endocarditis was actually due to the colon bacillus. The question might be put as to whether the bacterial endocarditis was primary and the renal abscesses secondary, but I think that is rather unlikely. The extent of the renal infection

was so great and its chronicity so evident that I am quite sure it preceded the endocarditis. Both popliteal veins showed thrombophlebitis, extending on the left up the femoral and iliac veins almost to the vena cava, but no emboli had broken off and there were no pulmonary infarcts. The lungs showed a rather diffuse pulmonary edema and very questionable early pneumonia, so I think that the signs observed for a period of six days were chiefly due to edema and not to pneumonia.

DR. ALFRED KRANES: What was the origin of the renal abscesses?

DR. MALLORY: I do not know. We see a significant number of cases of very severe diffuse pyelonephritis for which we never find anything to suggest the portal of entry of the infection. I think the majority of these cases run their course as cases of obscure sepsis, with not much evidence of renal insufficiency. This case was rather exceptional, since the symptoms of insufficiency predominated throughout the story. We have seen a number of cases of pyelonephritis almost as diffuse as this, with only slight terminal renal insufficiency.

DR. KRANES: This must have been going on for more than three weeks.

DR. MALLORY: Without any question. I should think it must have run back months at least. I should assume that the patient had been having renal insufficiency since the onset of the anemia and dyspnea.

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MEDICAL-COSTS INSURANCE BILL

House Bill No. 2301, sponsored by the Massachusetts Medical Society and designed to permit the formation of a corporation or corporations the function of which is to provide means of meeting the costs of medical care on a nonprofit insurance basis, was passed by both branches of the Legislature last week and was signed by Governor Saltonstall on May 22, the day of the celebration of the one hundred and sixtieth anniversary of the Society.

Permissive legislation having been granted, it now behooves the Society to take the necessary steps toward the formation of such a corporation and to devise rules and regulations, which must be submitted to the Commissioner of Insurance for approval. Much remains to be done, but at least the initial effort has had the support of the people of the Commonwealth.

ANNUAL MEETING

THE one hundred and sixtieth annual meeting of the Massachusetts Medical Society, the oldest state medical society in the United States with a continuous existence, was held at The Copley-Plaza, Boston, May 21 and 22.

The scientific exercises were conducted through the forenoons and afternoons of both days with an attendance exceeding the capacity of the accommodations. Space for the section meetings, which were conducted during the luncheon hour on May 21, was provided in other rooms or in other hotels. The record for general registration of members, 1525, is the largest in the history of the Society. The luncheon meetings of the sections were attended as follows: medicine, 148; obstetrics, 77; pediatrics, 56; dermatology, 53; anesthesiology, 34; radiology, 13; and surgery, 85.

This meeting was reminiscent of conditions twenty-four years ago, when the medical profession was adjusting its problems to the perplexities incident to an impending world war, for doctors throughout the nation are again grappling with the exacting demands of both military and civil service for preparedness in meeting the threatening conditions in connection with another world war. Because of this situation, the afternoon of the second day was given to the presentation of important phases of war surgery.

The business of the Council was carried forward with dispatch on the morning of May 21, so that the councilors were free to attend other exercises in the afternoon. The reports of standing and special committees, the appointment of new committees and the election of officers constituted the main items of business. The officers nominated and elected are as follows: president, Frank R. Ober, of Boston; vice-president, Edward P. Bagg, of Holyoke; secretary, Michael A. Tighe, of Lowell; treasurer, Charles S. Butler, of Boston; and orator, William B. Castle, of Boston. At the adjourned session on the following day, after the

adoption of the amendments to the by-laws by the Society, George L. Schadt, of Springfield, was elected to the newly created position of president-elect; he will become president at the close of the annual meeting in 1942. All the details of this meeting will appear in the official report to be published in an early issue of the *Journal*. On the evening of May 21, the members and their guests met for the annual dinner. After a few explanatory remarks and introduction of the incoming president and the guests from the other New England states, President Walter G. Phippen presented Dr. Nathan B. Van Etten, president of the American Medical Association. His address dealt with the situation confronting organized medicine and the practitioner at the present time, with the assertion that the physicians of this country must assume leadership in strengthening the courage and purpose of the people to maintain the American standards of civilization. Dr. Van Etten stated that with the drafting of men for military training and service, forty thousand doctors will be required, so that definite responsibilities rest with those in civil life in connection with home and hospital service and medical education. He paid well-deserved tribute to the American Medical Association for its organization and support of medical education and its assistance to the Government in various activities. He deplored the lay misconception of the position that this association occupies in serving the country and upholding the traditions of the profession. His appeal for loyalty to the nation and readiness for all to serve in every possible way in promoting the successful administration of the government was well expressed. Then, Dr. Frank H. Lahey, president-elect of the American Medical Association, was introduced. He emphasized the privileges of a democracy in its freedom of action, speech and the press for the individual and the minority, which is of great educational importance, but warned the audience that when the Government, after study of conditions and arguments, comes to the adoption of plans of action, all dissensions must cease and all agencies and individuals must unite in support of adopted plans; otherwise democracy will fail and disintegrate. These moving addresses should lead to a study of the arguments, facts and opinions expressed by these two able representatives of organized medicine.

After the adjournment of this meeting, the Society convened to hear the Shattuck Lecture by Dr. Alton Ochsner, of New Orleans, under the title "Thrombosis and Thrombophlebitis." The speaker discussed the etiology, pathology and treatment of the conditions included in the title in a fashion that clarified any misunderstanding about the disabilities, the results if untreated, and the benefits following approved methods of therapy. No ordinary reference to this lecture can give an adequate appreciation of the clear and forceful presentation of the subject. Fortunately the paper will be published, and can be enjoyed by all who are interested.

The program arranged by the Ladies' Committee was most successful. A total of 175 registered, and almost all participated in the scheduled events, which included tea at the Gardner Museum, dinner at the Ritz Roof, Hotel Ritz-Carlton, and a trip to and luncheon at the South Shore.

Forty-two fellows played one or more rounds of golf in the tournament at the Commonwealth Country Club.

The annual meeting of the Society convened at eleven o'clock on the second day. The first business was the report of the Secretary *pro tempore*, showing that the Society began the year with 5542 members and that in spite of 104 deaths, 17 retirements and 49 deprivations the net gain by readmissions and restorations was 97, bringing the membership to 5639. The amendments to the by-laws of the Society that had been approved by the Council were presented and adopted, and a vote of thanks to the Committee of Arrangements was passed in recognition of the well-arranged program. The President's report on the condition of the Society showed a normal growth of this body. After a warm tribute to Dr. Alexander S. Begg, the recently deceased secretary, he complimented the Treasurer for the able administration of his office, the committees for devoted service to the best interests of the corporation and the members of district societies for their

co-operation in matters pertaining to the general welfare of the Society. He impressed on the audience that much remains to be done to carry forward the useful functions of the Society in meeting the needs of the people of the State. He urged the creation of an executive committee of the Council, as defined in the by-laws, and the selection of an executive secretary, who would be of great assistance to the officers and committees of the Society. He then presented Dr. A. Warren Stearns, who delivered the Annual Discourse.* This address stands as a notable addition to the long list of papers read at annual meetings of the Society. Dr. Stearns led the audience through the history of evolution of the human race, in comparison with individual and collective experiences with a growing forest, and finally showed where the human race stands in its responsibility to meet the needs of all classes of the population. The address was well conceived, the main theme was skillfully handled, and enough wit and humor were interspersed to keep attention focused on the facts presented.

These sketchy references to a meeting of the Massachusetts Medical Society are designed not as tributes to the standing and accomplishments of this venerable society, for none are needed, but only as hints that careful study of the papers read during the session and of the action taken by the Council is incumbent on those members who are willing to share the responsibilities of maintaining the usefulness of this organization.

*Stearns, A. W. The role of the physician in a competitive society. *New Eng. J. Med.* 224:879-890, 1941.

TREATMENT OF BRAIN TUMORS IN CHILDREN

Modern therapy is founded upon accurate diagnosis. Abundant examples are found in current medical teachings. In the field of infectious disease the correct use of chemotherapeutic agents should be guided by accurate knowledge concerning the nature of the infectious agent. In the field of neoplastic diseases it has been recognized for many years that the most accurate and reliable method of reaching the correct decision concerning the nature of a suspected new growth is by gross and microscopic examination of an adequate sample of tissue. Lacking such a control, opinions concerning prognosis are open to grave questions, and evaluation of therapeutic procedures is practically impossible. Even more serious is the situation that occurs when the most successful means of treating a tumor are not used because of an incorrect conclusion concerning the nature of the neoplastic process. The unfortunate consequences of x-ray therapy based on inadequate diagnosis are illustrated by a paper in the present issue of the *Journal*. That the medulloblastoma is the only cerebellar tumor in infants and children has been a belief which has spread without proper support. It is possible that this impression goes back to Cushing's early work on medulloblastoma, which attracted wide attention, although he pointed out in a later paper the greater frequency of astrocytoma. In the series of brain tumors in infants and children cited by Ingraham and Campbell, the astrocytoma was actually found to be commoner than the medulloblastoma in the subtentorial region. An astrocytoma has a relatively good prognosis if removed surgically, but is not radiosensitive. A medulloblastoma is radiosensitive, and surgery, in addition to radiation, is the recommended treatment. But, even if the proportions of these two types were reversed, there is no justification for treatment of a tumor in a given patient on a purely statistical basis. Until a method is discovered of determining the nature of a new growth in a manner as accurate as that supplied by histologic examination, the generalization should be followed that no brain tumor, particularly in a child, should be treated by radiation therapy until surgical exploration has yielded sufficient material for histologic diagnosis of the tumor.

It has been only relatively recently that intracranial tumors of early life have been recognized in any considerable numbers. In the face of this distinct advance it would seem very unfortunate to lose opportunities for favorable results by instituting the wrong treatment, particularly when this treatment is based on incorrect statistical evidence.

MEDICAL EPONYM

Hodgkin's Disease

Thomas Hodgkin (1798–1866), pathologist at Guy's Hospital, London, wrote a paper, "On Some Morbid Appearances of the Absorbent Glands and Spleen," which was presented at a meeting of the Medical and Chirurgical Society of London on January 10 and 24, 1832, and printed in the *Medico-Chirurgical Transactions: Published by the Medical and Chirurgical Society, London* (17: 68–114, 1832). This treatise consists of a series of seven autopsy protocols and two case reports. Probable cases of tuberculous adenitis and leukemia were included in the series.

> It may be observed that notwithstanding some differences in structure, . . . all these cases agree in the remarkable enlargement of the absorbent glands accompanying the larger arteries; namely, the glandulae concatenatae in the neck, the axillary and inguinal glands, and those accompanying the aorta in the thorax and abdomen . . . this enlargement appeared to be a primitive affection of those bodies, rather than the result of an irritation propagated to them from some ulcerated surface or other inflamed texture through the medium of their inferent vessels. . . . Unless the word inflammation be allowed to have a more indefinite and loose meaning than is generally assigned to it, this affection of the glands can scarcely be attributed to that cause, since they are unattended with pain, heat, and other ordinary symptoms of inflammation, and are not necessarily accompanied by any alteration in the cellular or other surrounding structures, and do not shew any disposition to go on to the production of pus or any other acknowledged product of inflammation. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

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330 Dartmouth Street
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Separated Placenta and Eclampsia Associated with Cesarean Section and Followed by Death

A twenty-four-year-old para III was first seen at a clinic in the thirty-sixth week of pregnancy; the blood pressure was 190 systolic, 120 diastolic, and there was a large trace of albumin in the urine.

The two previous pregnancies had been uneventful: one terminated in a low forceps delivery, and the other was normal. There was no history of any disease.

The patient was treated for toxemia in a hospital for three days, after which she left the hospital against advice. She returned to the hospital a week later because of uterine hemorrhage and very acute abdominal pain. She was not in labor.

On physical examination the heart was not enlarged, and there were no murmurs. The lungs were clear and resonant; there were no rales. The uterus was enlarged to a size consistent with her dates and was spastic. The fetal heart could not be heard. A diagnosis of premature separation of the placenta was made, and cesarean section was decided on. While being prepared for operation, the patient had a severe convulsion. A classic cesarean section was performed after a transfusion of 200 cc. of citrated blood had been given. The fetus was stillborn. Two hours after operation the patient died.

Comment. Much of the disaster in this case can be attributed to lack of prenatal care, either because of ignorance on the part of the patient or because facilities for prenatal care of patients of the very low income group were unavailable to her. She did not appear at the clinic until she was in her thirty-sixth week, at which time she had a large trace of albumin and an elevated blood pressure. Medical treatment was immediately instituted, but the patient refused to remain in the hospital. If the seriousness of the condition were sufficiently impressed on this patient before she left the hospital, the subsequent convulsion can hardly be said to be the fault of the medical profession. However, the treatment, when the diagnosis of separated placenta was made, was not that which is generally recognized as the safest.

This patient apparently had a severe external hemorrhage, which is a condition not commonly associated with separated placenta. At operation the placenta was found to be entirely separated, a large clot lying between it and the uterine sinuses. The present method of treating such eclamptic patients is to rupture the membranes, pack the cervix and vagina tightly with sterile gauze, apply a Spanish windlass, and treat the convulsions conservatively. In Boston the use of magnesium sulfate and morphine is considered the safest procedure. Some clinics are using veratrum viride in cases of this sort.

This patient was poorly handled medically after the placenta separated and after the appearance of eclampsia. Had she stayed in the hospital and had her blood pressure not come down, induction of labor would undoubtedly have been decided on, and it is likely that the fatal result might have been averted.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

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Hodgkin's Disease

Thomas Hodgkin (1798–1866), pathologist at Guy's Hospital, London, wrote a paper, "On Some Morbid Appearances of the Absorbent Glands and Spleen," which was presented at a meeting of the Medical and Chirurgical Society of London on January 10 and 24, 1832, and printed in the *Medico-Chirurgical Transactions: Published by the Medical and Chirurgical Society, London* (**17:** 68–114, 1832). This treatise consists of a series of seven autopsy protocols and two case reports. Probable cases of tuberculous adenitis and leukemia were included in the series.

> It may be observed that notwithstanding some differences in structure, . . . all these cases agree in the remarkable enlargement of the absorbent glands accompanying the larger arteries; namely, the glandulae concatenatae in the neck, the axillary and inguinal glands, and those accompanying the aorta in the thorax and abdomen . . . this enlargement appeared to be a primitive affection of those bodies, rather than the result of an irritation propagated to them from some ulcerated surface or other inflamed texture through the medium of their inferent vessels. . . . Unless the word inflammation be allowed to have a more indefinite and loose meaning than is generally assigned to it, this affection of the glands can scarcely be attributed to that cause, since they are unattended with pain, heat, and other ordinary symptoms of inflammation, and are not necessarily accompanied by any alteration in the cellular or other surrounding structures, and do not shew any disposition to go on to the production of pus or any other acknowledged product of inflammation. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Separated Placenta and Eclampsia Associated with Cesarean Section and Followed by Death

A twenty-four-year-old para III was first seen at a clinic in the thirty-sixth week of pregnancy; the blood pressure was 190 systolic, 120 diastolic, and there was a large trace of albumin in the urine.

The two previous pregnancies had been uneventful: one terminated in a low forceps delivery, and the other was normal. There was no history of any disease.

The patient was treated for toxemia in a hospital for three days, after which she left the hospital against advice. She returned to the hospital a week later because of uterine hemorrhage and very acute abdominal pain. She was not in labor.

On physical examination the heart was not enlarged, and there were no murmurs. The lungs were clear and resonant; there were no rales. The uterus was enlarged to a size consistent with her dates and was spastic. The fetal heart could not be heard. A diagnosis of premature separation of the placenta was made, and cesarean section was decided on. While being prepared for operation, the patient had a severe convulsion. A classic cesarean section was performed after a transfusion of 200 cc. of citrated blood had been given. The fetus was stillborn. Two hours after operation the patient died.

Comment. Much of the disaster in this case can be attributed to lack of prenatal care, either because of ignorance on the part of the patient or because facilities for prenatal care of patients of the very low income group were unavailable to her. She did not appear at the clinic until she was in her thirty-sixth week, at which time she had a large trace of albumin and an elevated blood pressure. Medical treatment was immediately instituted, but the patient refused to remain in the hospital. If the seriousness of the condition were sufficiently impressed on this patient before she left the hospital, the subsequent convulsion can hardly be said to be the fault of the medical profession. However, the treatment, when the diagnosis of separated placenta was made, was not that which is generally recognized as the safest.

This patient apparently had a severe external hemorrhage, which is a condition not commonly associated with separated placenta. At operation the placenta was found to be entirely separated, a large clot lying between it and the uterine sinuses. The present method of treating such eclamptic patients is to rupture the membranes, pack the cervix and vagina tightly with sterile gauze, apply a Spanish windlass, and treat the convulsions conservatively. In Boston the use of magnesium sulfate and morphine is considered the safest procedure. Some clinics are using veratrum viride in cases of this sort.

This patient was poorly handled medically after the placenta separated and after the appearance of eclampsia. Had she stayed in the hospital and had her blood pressure not come down, induction of labor would undoubtedly have been decided on, and it is likely that the fatal result might have been averted.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

DEATHS

BIANCO — Joseph A. Bianco, M.D., of Boston, died May 23. He was in his sixtieth year.

Dr. Bianco received his degree from Harvard Medical School in 1904. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

DALY — William J. Daly, M.D., of Brookline, died May 17. He was in his sixty-ninth year.

Born in Boston, Dr. Daly graduated from the University of Berlin and received his degree from the Harvard Medical School in 1895. He was a former member of the Massachusetts Medical Society.

His widow, a daughter, two sons, three sisters and three brothers survive him.

FAIR — John F. Fair, M.D., of Cambridge, died May 20. He was in his seventy-third year.

Dr. Fair was physician for the Cambridge Latin School, and was a fellow of the American Medical Association and a member of the Massachusetts Medical Society.

FRAME — Joseph Frame, M.D., of Rockland, died May 24. He was in his seventy-sixth year.

Born in Shubenacadie, Nova Scotia, Dr. Frame graduated from Harvard Medical School in 1894. He was assistant examiner of Plymouth County, and was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, two daughters and four sons survive him.

McCARTHY — John C. McCarthy, M.D., of Malden, died May 22. He was in his seventy-third year.

Born in Lee, Dr. McCarthy graduated from Harvard Medical School in 1891. He was a former member of the Massachusetts Medical Society.

His widow, two daughters and two sons survive him.

NAVARRO — Vincente A. Navarro, M.D., of Medfield, died May 15. He was in his forty-sixth year.

Dr. Navarro received his degree from the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore. He was a member of the Massachusetts Medical Society and the American Medical Association.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATHS

LAMB — Zenas F. Lamb, M.D., of Keene, died April 28. He was in his seventy-seventh year.

Born in Athol, Massachusetts, Dr. Lamb graduated from Bellevue Hospital Medical College, New York City, in 1887. He was a member of the American Medical Association, the Cheshire County Medical Society and the New Hampshire Medical Society.

His widow, his mother and two brothers survive him.

MARKS — Homer H. Marks, M.D., of Berlin, was fatally injured on April 11 when he stepped into an old elevator well at the St. Louis Hospital in Berlin.

Born in Portland, Maine, in 1876, Dr. Marks graduated from Bowdoin Medical School in 1906. He was associated with the Mayo Clinic in Rochester, Minnesota, for several years.

Dr. Marks was a member of the Coos County Medical Association, the New Hampshire Medical Society and the American Medical Association.

Survivors are his widow, a son, and a daughter.

CORRESPONDENCE

HYPERTENSIVE HEART DISEASE

To the Editor: In the article, "The Development of the Concept of Hypertensive Heart Disease," by Drs. David Davis and Max J. Klainer, the statement appears, "In this country, Fahr was one of the first [1923] to appreciate the clinical significance of hypertensive heart disease."

The earliest worker in this field, if not the first, to mention, emphasize and reiterate the effects of arterial hypertension on the heart was Theodore C. Janeway (1872–1917). He mentioned it first in his book, *The Clinical Study of Blood Pressure* (1904). He reiterated it in 1906 (The diagnostic significance of persistent arterial pressure. *Am. J. M. Sc.* **131**:772–778, 1906), and reemphasized it in 1912 (A study of the causes of death in 100 patients with high blood pressure. *J. A. M. A.* **59**:2106–2110, 1912). His finest report on hypertensive heart disease, one that may be pointed to without question as the classic treatise on the subject, appeared in 1913 (A clinical study of hypertensive cardiovascular disease. *Arch. Int. Med.* **12**:755–798, 1913).

For reasons which are too extensive to consider here, but which are discussed by me elsewhere (Janeway on hypertension. *Bull. Hist. Med.* — in press), the excellent work by Janeway on the subject has frequently been overlooked and underestimated. I hope that this short note will aid in calling attention to his fine contributions on essential hypertension and hypertensive heart disease, which he so richly deserved.

The present war reminds us of his untimely demise. In the late autumn of 1917, after having had the general direction of the Division of Internal Medicine of the United States Army as his important assignment, Janeway made a personal investigation of the outbreaks of measles and pneumonia at certain cantonments. This, in addition to the energy required for the work at the office of the Surgeon-General in Washington and the biweekly clinics in Baltimore at Hopkins, weakened his power of resistance. Toward the end of December he became ill and after less than one week's illness of pneumonia, died at his home in Baltimore on December 27, 1917, at the age of forty-five. He was the first full-time professor of medicine at Johns Hopkins University School of Medicine under the William Welch Endowment, and served in this capacity from 1914 until his early death in 1917.

Nathan Flaxman, M.D.

3507 Lawrence Avenue
Chicago

REPORTS OF MEETINGS

GREATER BOSTON MEDICAL SOCIETY

A regular meeting of the Greater Boston Medical Society was held at the Beth Israel Hospital on March 4, with Dr. Aaron Thurman presiding. Dr. Ernst P. Boas, of Columbia University College of Physicians and Surgeons, spoke on "Factors That May Induce Cardiac Infarction." It was stated that in this condition, sugges-

tions for further clinical and laboratory studies should be the result of clinical observations.

Dr. Boas discussed first the relation of chest trauma to coronary thrombosis. That thoracic blows may be sufficient to induce heart attacks has been accepted, but the mechanism is still uncertain. There may be either direct injury to the myocardium or an indirect effect on the coronary vessels through pressure from hemorrhage.

The relation of exertion to coronary infarction has been a constant source of discussion in medicolegal as well as medical circles. Dr. Boas cited several cases of angina pectoris or coronary thrombosis occurring originally with or concomitant to unusual or sudden physical stress. Angina pectoris may definitely be inaugurated at the time of sudden exertion, and may persist while the patient continues to work. As to whether this may be considered a cause for disability, Dr. Boas suggested that each case must be considered separately. It is believed that physical exertion may be a definite cause of coronary attacks, especially if the signs and symptoms are immediately noted. Although the subsequent onset may be suggestive when occurring within a few hours or days, one cannot be sure in such cases. In some states, the onset must accompany an unusual effort or accident.

The well-known relation of emotion to coronary thrombosis and angina pectoris is a clinical observation for which there has been no adequate explanation. Sudden death may result from ventricular fibrillation following a sudden outpouring of adrenaline, or a temporary relative myocardial ischemia would make this analogous to physical effort.

Although the causative relation of allergic conditions to coronary-artery disease is still controversial, there now appears to be definite evidence in favor of such a connection. That similar changes occur during anaphylactic shock in animals and in angioneurotic edema has been demonstrated. Occasional cases of anginal attacks have been observed in the process of desensitizing allergic patients, and the role of nicotine in inciting coronary changes is not unusual. Reversible changes in the electrocardiogram are present during certain asthmatic attacks.

The effect of cold has often been investigated, and it has been found that cooling from any cause may induce coronary attacks, possibly by reflex coronary-artery spasm. Dr. Boas believes that cold weather and snow definitely increase the incidence of heart attacks. The immersion of the hands of a susceptible person in ice water may induce immediate inversion of the T wave of the electrocardiogram and may cause a coronary attack.

Certain other conditions that may contribute to coronary-artery accidents are grippe and other debilitating diseases, postoperative states, hemorrhage and shock, insulin shock, electric shock, high altitudes with incident anoxia, and excessive heat and humidity. Physicians may often scoff at these external factors, yet they invariably warn against them in practice. The most plausible explanation for coronary occlusion and myocardial insufficiency seems to be that arteriosclerosis narrows the available vascular channels and that reflex spasm may cause a similar temporary diminution of blood flow. Under these conditions, such external factors, which would have no effect on a normal heart and coronary system, are sufficient to cause a temporary or permanent impairment of myocardial nutrition, with subsequent signs and symptoms of coronary thrombosis or angina pectoris.

The discussion was opened by Dr. Herrman L. Blumgart, of the Beth Israel Hospital, who stated that although he had no fundamental disagreement with the thesis of Dr. Boas, he believed that everyone puts some additional burden on the heart every day or week, which might well inaugurate a coronary attack. It is only when definite signs of immediate myocardial insufficiency are manifest that one is justified in assigning any causative role to the exertion. Many of Dr. Boas's clinical observations have been corroborated at the Beth Israel Hospital, where experiments have been carried out on exercise in cold rooms and in warm rooms with ice cubes in the patient's hands. It was stated that careful questioning usually elicits a definite coronary background in most cases of attacks induced by external factors except direct trauma.

Dr. Samuel A. Levine, of the Peter Bent Brigham Hospital, discussed coronary-artery disease under the headings of predisposing and precipitating factors. Of the former, all that is known concerns the definite role of heredity, sex and any disease with atherosclerosis — such as diabetes, myxedema, gout and thromboangiitis obliterans. The male sex predominates 3:1 in general, and 24:1 under forty years of age. Among the precipitating factors, effort easily leads in importance. Since the average person spends twenty times as much time sleeping or resting as in an active state, the incidence of heart attacks, which is twice as large while at rest as while exercising, indicates that when a correction is made effort surely plays an important role. Dr. Levine believes that although immediate exertion is undoubtedly harmful, subsequent graded effort may be helpful, probably by reestablishing an adequate auxiliary circulation. The inadvertent intravenous use of adrenalin has been known to cause coronary occlusion, and it was suggested that one act accordingly rather than wait for convincing proof that an outpouring of adrenaline is harmful.

The next discusser was Dr. Samuel H. Proger, of the Joseph H. Pratt Diagnostic Clinic, who emphasized that the unusual cases in which exertion in convalescent cardiac patients is not harmful should not lead one to adopt that as a standard or even advisable form of treatment. Whether angina pectoris is followed in a large percentage of cases by coronary thrombosis is apparently dependent on the astuteness of the questioning physician, as shown by a comparison of statistics from clinic patients and from private patients of reputable cardiologists. It was stated that the finding of unexplained rapid sedimentation rates in suspected cases may presage a coronary attack by weeks or months and that such findings are not common.

Dr. Monroe J. Schlesinger, of the Beth Israel Hospital, reminded the group that coronary-artery disease is a question of supply and demand. In regard to compensation, he pointed out that the same job day in and day out is not the same job, for it is being done by a different man. A gradually decreasing coronary supply with increasing age is a physiologic fact. Furthermore, the degree of unpreparedness probably plays a part in determining the ill-effects of unusual or sudden effort.

The discussion was closed by Dr. Boas, who suggested that preceding coronary-artery disease is probably invariably present despite the lack of clinical manifestations. He is of the opinion that bedrest should be urged for as long as possible, and he advises four to six weeks, even in so-called "favorable cases." The addition of infarction may be of benefit to the patient by eliminating the offending artery. Enforced rest as obtained in arthritis and cerebral vascular accidents aids in diminishing coronary attacks. The danger of ingesting large meals was emphasized. Finally, Dr. Boas stated that at least part of the apparent increase of coronary disease is due to better diagnosis.

BOSTON ORTHOPEDIC CLUB

At a regular meeting of the Boston Orthopedic Club on March 17, Dr. Philip D. Wilson spoke on "Recent Experiences in England." In introduction, Dr. Wilson reviewed the background for the American Hospital in Britain. He then went on to discuss the four kinds of explosives used by the attacking forces and their different effects on property and human beings. Several patients were admitted without obvious external injuries and poorly understood neuromuscular derangements. One group developed a peripheral paralysis similar to that of poliomyelitis except in its rapid clearing. Another group developed paraplegia, which also ran a short self-limited course.

Air-raid defense was briefly discussed. Experiences in the recent Spanish War proved the advantages of using bomb shelters more generally and of making more adequate shelters when possible. Although they are often inadequate, the shelters in England usually protect against any but direct hits. The subways, which originally were not supposed to be used and in which the hygienic conditions were at first atrocious, are now being rather generally employed as shelters, and the government has made surprisingly rapid and effective improvements. Whereas the workers formerly used the shelters quite often, it is now considered not only patriotic but practically as safe to continue their commuting and work with only temporary intermissions at the most. Daytime raids at best have been ineffective. Antiaircraft defense, although improving with better and more widespread radio detection, still leaves much to be desired. The new night fighters offer promise for better protection. An important item has been the use of decoy airdromes and hangars to draw enemy fire and thus waste ammunition on barren countrysides. Among the more important defense groups are the bomb demolition squads, who combine ingenuity with courage in finding and inactivating time bombs. It is interesting from a medical standpoint that auscultation is freely used to determine the presence of timing devices within a bomb and that freezing with carbon dioxide is one method of preventing the explosion of chemically constructed bombs.

Medical co-ordination is under the Ministry of Health. An emergency medical service for the development of medical units employs laymen rather than physicians. It is their duty to establish hospitals and evacuate people from danger zones. Unused hospitals and asylums have been reopened and renovated where possible, and some new hut hospitals have been constructed. In London the defense zones are pie-shaped sectors running out from a large medical school or teaching hospital in the city and extending out forty or fifty miles in gradually widening areas. The local doctors are under military orders; their salaries are small but much better than could be obtained from the poor practices that are now possible.

The American Hospital in Britain has its headquarters in an old asylum that is well heated but has comparatively poor surgical facilities. There are 1500 beds, of which 300 belong to this group. There is a large British staff, with three surgical services. This institution is the base hospital for three sectors and the evacuation center for southeastern England, especially Portsmouth and Southampton. A good supply of fresh blood, liquid plasma and dried serum is available. Those admitted to the hospital consist of two groups: any uniformed man — these make up about two thirds of the total — and civilians who are injured by the enemy, injured in civilian defense or have been under treatment in a hospital evacuated because of enemy bombs.

The type of work done by the general surgeon is largely hernias, interval appendectomies and vascular operations. The plastic surgeons, under Gillies, have been especially concerned so far with aviators, whose hands and faces are apt to be severely burned in escaping from burning planes. It has been found that tanning of these areas does more harm than the burns themselves. This is especially true of the hands, where the eschar interferes with the circulation. It also has a tendency to require too long immobilization of the hand and face muscles. The neurosurgical service has thus far been relatively inactive. The orthopedic service, on the other hand, has been busy treating fractures and other injuries, including those of many survivors of the Battle of Dunkirk.

During raids, patients are brought to first-aid centers by ambulances and are admitted by the senior surgeon for appraisal and decision about the type of treatment. The first group of patients, classified as urgent, are treated for shock with plasma and intravenous fluids. There are always one or two teams in the shock room. The second group, considered capable of immediate operation, are sent to the operating rooms after x-ray examination. Their wounds are débrided, and sulfonamides are usually employed locally. The majority of wounds are packed open, primary suture being carried out only when the patient can be followed by the original operator for the next seven to ten days, which is very unusual. The Thomas splint is being employed less than previously. There is now a definite trend toward the Orr method. There is often poor apposition of fragments, and the original fixation must be changed when the base hospital is reached. The third group consists of those with minor wounds, which are dressed; these patients are then sent to the wards.

It is characteristic of the wounds that there is a great prevalence of shock without obvious blood loss. Clinical judgment has largely supplanted determinations of blood pressure, protein levels and hematocrit readings in evaluating the status of a patient. In the surrounding countryside, emergencies are only too often seen by inexperienced men in small towns whose treatment is often ill-advised. In any questionable case of shock the patient should be established in the shock room, and the problem of infection should be only a secondary consideration.

The patients arrive at the base hospitals from a few days to several weeks after the original injury. The wounds are usually grossly infected, and it is too late even to consider surgical cleansing. Most wounds are multiple because of the multitude of secondary projectiles. The wounds are usually small on entrance and comparatively large on exit. Gas-bacillus infection is very common, but gas gangrene has been infrequent. Many wounds that have been inadequately treated must be left alone because of the danger of increasing or causing a flare-up of infection. About two thirds of all patients required revision of their original orthopedic result. They are taken to the operating room, where the wounds are opened under general anesthesia, sulfathiazole in doses of from 5 to 7 gm. being introduced into the wound. This drug is usually administered orally on the succeeding days. Because of the high incidence of comminution in the fractures, traction is usually necessary following reduction. For this purpose the Roger-Anderson or Haynes apparatus has been widely used.

Comparison was made with treatment of similar wounds in the last war. The patients do very well on the whole, with only moderate elevations of temperature for a few days. Symptoms are usually employed as the indications for changes in therapy, and the drug dosage is controlled

by blood-level determinations. Pain and anxiety are largely absent, compared with patients treated by the Carrel–Dakin method; there is much less work for the medical staff, and better continuous position of the bone fragments. Under the present regimen, only 2 of 90 patients required daily dressings, and these were minor enough to be carried out by nurses. Dressings are not changed for about a month unless absolutely necessary. The odor naturally becomes very strong, but fortunately the British like the open air, and new charcoal bags are being used to absorb a large part of the smell. The first dressing is carried out under general anesthesia without any disturbance of traction.

The end results, even including cases of gas infection, compare favorably with those of the last war. It is believed that chemotherapy probably has a good local bactericidal effect. Serum has been used only on occasion, but it is thought that combined therapy is undoubtedly the best for gas-bacillus infection. If crepitation is present without gangrene, the area is incised and treated like the other wounds. There has been only one amputation, which is a marked improvement, although there may be others later. Success is attributed to the local rest afforded the wound, which favors local-tissue defense, the constant pressure, which aids the circulation, and especially the absence of contamination. For it is now known that hospital infection is altogether too high, especially where many daily infected dressings are done. It has been shown experimentally that merely turning back the sheet over an infected wound will cause a heavy growth of the pathogenic organisms on Petri dishes placed within twenty-five feet of the bed.

Unsolved problems consist of persistent osteomyelitis and delayed union or nonunion. But even if later amputations are necessary, they become elective rather than emergency measures. Nerve injuries subsequent to sinus tracts often hinder therapy, and it has been found best to do a wide resection of the infected area, with later repair of the nerve and bone grafts.

Erratum. In the report of a meeting of the Harvard Medical Society, contained in the May 15 issue of the *Journal*, the phrase "a guanidine compound" in line 36 of the second column on page 874, should read "a pyrimidine compound (sulfadiazine)."

NOTICES

JOHN T. BOTTOMLEY SOCIETY

The regular monthly meeting of the John T. Bottomley Society will be held in the Out-Patient Department Building of the Carney Hospital on Tuesday, June 3, at 11:30 a.m. Drs. Timothy F. Lyons and Charles H. Dustin will speak on "Intestinal Intubation."

Physicians and medical students are cordially invited to attend.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

The annual dinner outing of the Norfolk South District Medical Society will be held at the South Shore Country Club on Wednesday, June 11. There will be an afternoon bridge and tea for the ladies and golf for the doctors. Dinner will be served at 7 p.m. followed by an entertainment.

EXAMINATIONS FOR APPOINTMENTS IN THE MEDICAL CORPS OF THE UNITED STATES NAVY

The next examination for appointments as assistant surgeon (lieutenant, junior grade), United States Navy Medical Corps, will be held at all major Medical Department activities on August 11 to 15, inclusive. Applications for this examination must be received at the Bureau of Medicine and Surgery, Navy Department, Washington, D. C., not later than July 15.

Applicants for appointment as assistant surgeon must be citizens of the United States, more than twenty-one but less than thirty-two years of age at the time of accceptance of appointment, and graduates of a Class A medical school who have completed at least one year of intern training in a hospital accredited for intern training by the Council on Medical Education and Hospitals of the American Medical Association.

A circular of information listing physical and other requirements for appointment, subjects in which applicants are examined, application forms and other data pertaining to salary, allowances and so forth may be obtained from the Bureau of Medicine and Surgery on request.

An examination for appointment as acting assistant surgeon for intern training in naval hospitals accredited for intern training by the Council on Medical Education and Hospitals of the American Medical Association will be held at all major Medical Department activities on June 23 to 26, inclusive. Students in Class A medical schools who will complete their medical education this year are eligible to apply for these appointments, and if successful will receive their appointments approximately after the date of the examinations. Students in Class A medical schools who will have completed their third year of medical education this year are eligible to take this examination, and if successful will receive their appointments on or about July 1, 1942, after they have completed their medical education.

Applicants for appointment as acting assistant surgeon for intern training must be citizens of the United States, more than twenty-one but less than thirty-two years of age at the time of acceptance of appointment. Acting assistant surgeons are appointed for a period of eighteen months. After the appointee has served as an intern in a naval hospital for twelve months, he is eligible for and may take the examination for appointment as assistant surgeon.

A circular of information listing physical and other requirements for appointment as acting assistant surgeon, subjects in which applicants are examined, application forms and so forth may also be obtained from the Bureau of Medicine and Surgery on request.

Assistant surgeons and acting assistant surgeons for intern training are appointed in the rank of lieutenant (junior grade), United States Navy Medical Corps. The pay and allowances for an officer of this rank total $2699 per year if he has no dependents, and $3158 per year if he is married or has dependents.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, June 1

Monday, June 2

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, June 3

*11:30 a.m. Intestinal Intubation. Drs. Timothy F. Lyons and Charles H. Dustin. John T. Bottomley Society. Out-Patient Department Building, Carney Hospital.

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater

WEDNESDAY, JUNE 4

•12 m. Clinicopathological conference. Children's Hospital.

THURSDAY, JUNE 5

7:15 p.m. Lecture on Cancer. Dr. Herbert L. Lombard. New England Hospital for Women and Children.

•Open to the medical profession.

MAY 30, 31 — American Heart Association. Hotel Statler, Cleveland.

MAY 30–JUNE 2 — American College of Chest Physicians. Hotel Statler, Cleveland.

JUNE 2 — American Medical Golfing Association. Page 785, issue of May 1.

JUNE 2–6 — American Medical Association. Cleveland.

JUNE 2–6 — Woman's Auxiliary, American Medical Association. Hotel Carter, Cleveland.

JUNE 4 — Harvard Medical Alumni Association. Page 790, issue of May 1.

JUNE 22–24 — Maine Medical Association. Marshall House, York Harbor, Maine.

OCTOBER 13–24 — 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

OCTOBER 14–17 — American Public Health Association. Page 579, issue of March 27.

DISTRICT MEDICAL SOCIETY

NORFOLK SOUTH

JUNE 11 — Page 961.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Introducing Insects: A book for beginners. By James G. Needham, Ph.D. 12°, cloth, 129 pp., with 86 illustrations. Lancaster, Pennsylvania: The Jaques Cattell Press, 1940. $1.50.

Man on His Nature. By Sir Charles Sherrington, O.M. The Gifford Lectures, Edinburgh, 1937–8. 8°, cloth, 413 pp. New York: The Macmillan Company, 1941. $3.75.

Proctology for the General Practitioner. By Frederick C. Smith, M.D., M.Sc. (med.). 8°, cloth, 466 pp., with 161 illustrations and 5 colored plates. Philadelphia: F. A. Davis Company, 1941. $4.50.

The Periodicity and Cause of Cancer, Leukaemia and Allied Tumours, with Chapters on Their Treatment. By J. H. Douglas Webster, M.D., F.R.C.P.E., F.F.R., honorary director, Meyerstein Institute of Radiotherapy, Middlesex Hospital, London, lecturer and examiner in radiology, University of London, and examiner in radiotherapy, Faculty of Radiologists, London. 8°, cloth, 178 pp., with 5 plates, 8 charts and 8 tables. Baltimore: Williams and Wilkins Company, 1940. $3.50.

A Laboratory Manual of Physiological Chemistry. By D. Wright Wilson, Benjamin Rush Professor of Physiological Chemistry, University of Pennsylvania. Fourth edition. 8°, cloth, 298 pp. Baltimore: Williams and Wilkins Company, 1941. $2.50.

BOOK REVIEWS

Chirurgie réparatrice et correctrice des téguments et des formes. By L. Dufourmentel. Preface by Professeur Pierre Sebileau. 8°, paper, 408 pp., with 451 illustrations. Paris: Masson et Cie, 1939. $3.00.

The author has been well known for his work in reparative and plastic surgery since World War I. In this volume, he has embodied his methods of approach to various deformities of the face. He has not attempted to deal with the treatment of other parts of the body, except corrective surgery for hypertrophied breasts. War injuries, as well as civilian injuries, are covered, which is of great importance at this time.

In the first chapter, the author discusses general methods of repair, and gradually elaborates the surgical technic applied to various structures of the face. The chapter on deformities of the nose is more fully covered than those of the eyelids, ear and lips. The discussion of the repair of war injuries is interesting and has historical value, but the results obtained do not measure up to the present standards of reconstructive surgery. Reparative surgery has made much progress in the last twenty-five years and better results may therefore be expected in the repair of fractures and war injuries.

On the whole, there is much that is well discussed and instructive. The author's style is simple and direct, and the illustrations are abundant and clever. It is a valuable contribution to the literature of reparative surgery of the face, and will interest those who are in this branch of surgery, as well as those in general surgery.

The Chronicle of Crichton Royal (1833–1936). By Charles Cromhall Easterbrook, M.D., F.R.C.P. (Eng.). With a foreword, "Some Early Crichton Memories," by the late Sir James Crichton-Browne, M.D., LL.D., F.R.S. 4°, cloth, 663 pp., with 103 illustrations and 1 map. Dumfries, Scotland: Courier Press, 1940. 25 sh. net.

This large book is a detailed history of one of the famous mental hospitals in Scotland, covering a period of over one hundred years. The first report of the hospital was issued in 1840. The founder was James Crichton, who studied at the University of Edinburgh, and while still a youth went to India, in the service of the East India Company. He became physician to the Viceroy, but also found time to make a fortune by trading in India and in China, and returned to Scotland in 1808, when only forty-three years of age, a rich man. It was with this fortune that he endowed the Crichton Royal Institution, a hospital staffed with the best of Scottish physicians for over one hundred years. The book is fully illustrated with photographs and portraits, and there is an extensive index. It forms a record of enduring work.

A Handbook of Hearing Aids. By A. F. Niemoeller, A.B., M.A., B.S. Foreword by Harold Hays, M.D. 8°, cloth, 156 pp. New York: Harvest House, 1940. $3.00.

This is a description in nontechnical language of the different types of hearing aids and the methods of using them to best advantage. At the end of the book, there is a complete list of hearing aids and the companies that manufacture them. This book should be in the office of all otologists who are interested in treating the deaf and aiding them by means of hearing apparatus.